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VOLUME IV *October, 1956* NUMBER 10

PANEL DISCUSSION ON SOME PSYCHOLOGIC AND PSYCHIATRIC PROBLEMS OF OLD AGE*

Moderator:† EDWARD B. ALLEN, M.D.

Panelists:‡ HOLLIS E. CLOW, M.D., WILLIAM C. OFFENKRANTZ, M.D. AND CLARK TIBBITTS

MODERATOR ALLEN: In introducing the subjects to be discussed by the Panel, which have largely to do with the role of the psychiatrist in handling geriatric problems, it is important to outline what is meant by instincts, instinctive drives, motivations, and emotions.

Each decade of the human life span has its own emotional problems and its moments of uncertainty, which vary to some degree from those of the preceding and subsequent decades. In considering instincts, it is important to remember that all human beings, if they live long enough, pass through two periods intimately concerned with instinctive drives. In these periods, they frequently feel insecure; emotional tensions arise, which can be relieved through knowledge of their etiology. The approach to these problems should be conservative and temperate. The two periods are those of puberty and involution.

At puberty, the instinctive drive for propagation, or race preservations, is more or less quickly and consciously superimposed upon the previous instinctive drive for self-preservation which promotes growth, development, and self-defense. Although a degree of these drives is biologic, the method of expression is amenable to psychologic influences. A conflict often arises in youth between these two instinctive drives. If this conflict becomes too acute, it leads to perplexity and undue self-consciousness. The victim seeks relief in withdrawal from the realities of life, avoids the responsibilities of reproduction, and may build up a delusional defense against them. Such reactions are frequently schizophrenic in character.

In the involutional period, the more or less adequate adjustment between

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the instinctive force of self-preservation and race preservation maintained through middle life is no longer adequate. The establishment of a new psychologic adjustment and psychologic attitude is imperative for the equanimity of the mind and body. The instinct for race preservation abates somewhat reluctantly in the more fundamental drive for self-preservation, which now asserts itself more consciously. The altruism and generosity which grew out of the desire to preserve the race and to think of others also abates to some degree.

The person passing through this involutional period becomes more jealous of his earthly possessions and aware of the integrity of his body. As he becomes more conscious of self, he is frequently less conscious and less concerned about others. He begins to appreciate and to fear that he is aging. He resents the inevitableness of change. He speculates on how many years of life are left to him. He faces the future with mixed feelings. He is now forced to alter his philosophy and his former conditioned pattern of response.

If he becomes appreciably apprehensive or disturbed, his personality disorder is usually emotional and depressive in character rather than schizophrenic. He may distort reality and exaggerate his inadequacies, but he does not replace his environment entirely with one of his own fantasies.

These instinctive problems are closely interwoven with the emotional responses of personality. It is through these emotional responses that behavior is influenced. It betrays how successfully an individual is reacting to the aging process.

Generally, the first indication of senescence occurs between 50 and 60 years of age. The aging individual awakens suddenly to an extraneous stimulus in the early hours of the morning when things are quiet. He reflects on recent experiences and recalls that he is growing old. A sequence of events has transpired to promote this.

He appreciates that he fatigues more easily. He is more exhausted after a hard day's work. When he stays out late at night, he feels it more the next day and is less efficient. A younger man has passed him on the stairs. When hustling for a train or other means of conveyance, he breathes rapidly for some moments after he has reached it.

When his wife asks him to accept an invitation to dinner or to go to the movies after he arrives home for the evening, he is irked. He thinks how much more comfortable it would be to doze over his newspaper before the fire in dressing gown and slippers.

Recently, the barber told him he was getting thin over the temples and more gray over the ears. His bushy eyebrows were trimmed and protruding hairs were snipped from his nostrils and ears. As he left, he was helped with his coat.

Walking on the street with his son, the latter observed him glancing at an attractively dressed young woman and cautioned, "Why don't you be your age; you are getting too old for such things, Dad."

He overhears children playing on the street and warning one another not to bump into the old fellow. Of late years, he has had to have his glasses changed in order to enjoy the movies. At the theater, he has had to obtain seats in the

front row of the orchestra in order to hear the dialogue and catch the significance of the risqué jokes.

The dentist has advised the removal of his remaining pivot teeth and decayed molars. A complete set of dentures would be more comfortable and remove the chance that a latent infection is the cause of the recent pains in his shoulders or knees.

The tailor notices that his girth has increased and suggests size 42 instead of 40. A physician has recommended a gastrointestinal x-ray series for the increasing constipation, or has referred him to a dermatologist for that small dry area on his forehead that persists in scaling and remaining moist.

More important than all these, when the physician took his blood pressure, he was told that he must reduce his diet, take things easier and, above all, not worry.

I present that emotional picture so that you will have some understanding of the way the older person feels, and what is going on in his mind, when he sees a physician. These things may sound somewhat humorous because they are on the other fellow, but they are all apt to pertain to us as we grow older.

The initial complaint indicating senescence is that of fatigue, an inability to function as efficiently or as rapidly as before soon follows. It takes the older person longer to recuperate than when he was younger.

The biologic facts tend to precede the psychologic. The latter arise out of the attitude toward senescence. At this point, I want to call on Dr. Offenkrantz, and ask him if he will tell us about the role of the psychiatrist in the handling of these geriatric problems and the way in which we try to help the patient with his instinctive drives and his emotions.

DR. OFFENKRANTZ: Thank you, Dr. Allen.

It might be worthwhile to approach the problems of the aged, not from the standpoint of the psychiatric specialist but from that of practitioners of medicine, because they have the first, the greater, and often the only job to do in this area.

One aspect of the problem that strikes me as fruitful is the reference Dr. Wilson made in his paper to aging as an era of second childhood. I believe that this has some implications for physicians in dealing with geriatric patients.

I refer particularly to the problems of childhood when regarded in an adaptational frame of reference. This is either a parochial or a theoretical position, depending upon who is talking with you. At any rate, within this framework, anything that promotes survival is adaptive. Anything that does not promote survival is maladaptive. According to this orientation to the problems of human growth and development, the human instincts are considered to be two—sexual and assertive. For children in our society the second of these produces a conflict. On the one hand is the child's essential biologic dependence upon the parent which, in our culture particularly, is prolonged long after it is biologically necessary, because of such requirements as education and economic survival. On the other hand is the child's innate tendency to grow and differentiate, to assert himself, and to become independent of his parents.

In the aging period the capacity for independent self-assertion begins to diminish on a physiologic basis as well as in relation to that aspect of it which stems from the feeling of being needed by children and grandchildren.

At the same time, the older person's dependent satisfactions derived from being needed by a growing family are also diminished as the offspring grow up and away.

In the early part of this century, it was considered appropriate for three generations to live out their lives simultaneously under one roof. However in the 1950's this form of the American family structure, particularly in urban areas, has become rarer. Consequently, when the aging person loses the grand parental role, *i.e.*, to help the parents and to help raise the grandchildren, he loses a role in which he has experienced both assertiveness and dependence.

I should like at this point to emphasize that these emotional problems frequently masquerade as physical difficulties, including structural pathology, and that to elicit the underlying problem may be difficult. This, in part, is because the aging person may feel humiliated to reveal his feelings.

From this you can see what the rationale might be for a practical way of handling the aging patient who comes to a physician. Especially when assertive capacities begin to fail, these people need, above all else, the same thing a child does. They need to have the kind of dependent relationship with you that a child has with its parents. They need to feel appreciated, cared for, and important.

To make the story even longer, let us take a different kind of example as in the case of a geriatric patient who was deprived during his childhood of this kind of consistent tenderness—which can be demonstrated as one of the things a child needs in order to live and to grow. Can you give it to him? Will he be able to use it? The answer for practical purposes is no, probably not. It is a relationship he cannot use if he has never before had it.

There is something else you can do for these people, however. You can give them the opportunity for a relationship with a person in authority with whom they can "fight." I refer you again to the childhood of such persons. The child who cannot elicit, because of his parents' difficulties, tenderness sufficient unto his needs, will probably be a child who will either withdraw completely or learn to fight. If he learns to fight with his parents and the community in response to the frustration of his dependency needs, he may continue to do so throughout life. When such a person as this is again faced with the new stress of the aging period, he is lost. He cannot turn to anyone for the dependent relationship which he never knew in childhood, because he does not know how. What he can do, however, is to find a person who will allow him the importance of being quarrelsome, who will allow him to be demanding and contentious and unconsciously dependent. If he can find such a person in his physician, I believe this is an appropriate role for the physician.

MODERATOR ALLEN: Mr. Tibbitts, can you tell us a little more about some of the environmental influences and be more specific with regard to them?

MR. TIBBITTS: Dr. Allen, when I was talking from the other side of the plat-

form, I was trying to describe some of the changes that have taken place in society. Now, I should like to turn to the individual.

Sociologists and social psychologists have been concerned, as Dr. Allen has indicated, with determining some of the basic lifelong desires. I should like to begin by extending the list that we have already heard.

One, on which there is fairly general agreement, is the lifelong need for the opportunity to associate with other people, to express some of the kinds of feelings that were just described. Another is the need to be creative in some way or another, the need to have the feeling of making a contribution effective in improving the environment in which he lives. Others are a strong desire for security; a desire to retain the tie to the family, or to the society in which the individual was nurtured; a desire, as mentioned in Dr. Wilson's paper, for individuality; a feeling that "I amount to something, I count, I am a person, an individual"; and the feeling of a need for a frame of orientation, for some understanding of the meaning of life, some effort to appreciate or to have a recognition of a plan of society and a place in it. The last becomes increasingly strong in the older person as he is moved out of the roles that he has enjoyed earlier.

The important thing is that these are lifelong desires or basic needs; in earlier societies the means of satisfying them were present. They had been worked out over hundreds of thousands of years. Earlier cultures developed ways of meeting these needs of the individual. The large-household family group was one of the adaptations that was useful, and it satisfied a number of these needs. People worked, as I indicated earlier, all of their lives and had a work role or a useful role. An obviously useful role in society was also a means of satisfying some of these needs.

People lived in small groups, in what we call in sociologic language the primary group, in which they had day-to-day contacts with people with whom they felt free and upon whom they could call for assistance. In this kind of preindustrial society, there was little of the segregation that was mentioned in Dr. Wilson's paper and that has become a problem for many older people today.

In primitive society, and even in our own society as long as we were primarily an agricultural and handicraft society, the older person tended to acquire more prestige as he grew older. Sometimes he was given prestige by the group; sometimes he took it. He was able to establish himself and maintain himself as a person of authority and value in the community.

This has changed, because we spend a smaller part of our lives working. The large family group has broken down. Urban living is much more anonymous, and contacts are much more casual and impersonal than was life in the small rural community.

It seems to me that if the wall of segregation that has been growing is to be broken down, the essential challenge is to find new occupations. I do not mean, essentially, gainful employment, but new ways of spending time that will replace the time and effort that we put in as parents and as members of the work community.

The majority of people beyond 60, 65 or 70 years of age are not going to be

in the work force. The parental role ends for most people at some time between 45 and 55 years of age. A woman whose career has been that of mother is to a large extent retired at that point and needs a new reason for existence.

How to develop new roles that satisfy the need for a feeling of creativity, that give security, that give individuality, and that give an individual meaning, is the great challenge. It is not a matter of making the person *feel* that he is wanted or useful, but it is a matter of *making* him useful and wanted.

To a large extent, this will probably entail a change in our attitudes, or a change in our culture. In essence, it means that we must recognize that we are moving into a civilization in which leisure time is a far more important part of our lives than it has been in those of any earlier generation. We have to recognize people and give people status for spending time in such things as further education, various kinds of creative activity, and voluntary service.

If we can do these things, it seems to me that there is an opportunity to enable older people to continue to meet their needs and to continue close human associations.

When children are gone, when a spouse dies, when associations on the job are broken through retirement, a great many people lose their contacts and need to find new ones. Certainly, the physician is not going to be around twelve or fifteen hours a day to provide this outlet for the individual who wants to be quarrelsome or expressive in some other way. Hence, other kinds of opportunities must be developed besides visits to the physician's office.

MODERATOR ALLEN: In handling this problem, we try to talk about what to do for the individual, but we have to recognize the fact that the individual is failing, and that there is a diminution in his visual and auditory acuity. Under such conditions, he sometimes becomes embarrassed, builds up defenses, and becomes more or less disarticulated with society.

Some of his emotional defenses under these conditions manifest themselves in somewhat the following way, as was well brought out by Gittelson some time ago in a paper in the *Journal of the American Geriatrics Society*. He stated that at first there may be a decreased memory for recent events. He interpreted this as possibly a turning away from the painfulness of the present. Then there is a sharpening of memory for the past, especially when life was successful. There is a more self-assertive attitude as compensation for insecurity. There is a mild depression due to isolation and a feeling of loneliness. There is an introversion, an increased sensitivity with querulousness and paranoid attitudes, and finally a free-floating anxiety caused by death among persons in the same age group, especially when relatives or friends are involved.

These things are important to remember. I have known Dr. Clow for many years. He is inclined always to strike an optimistic note. After presenting these challenging facts, I am going to ask him something about the stresses of aging individuals and what happens to them in spite of these stresses and the defense reactions that I have mentioned.

DR. CLOW: This discussion has been of interest to me, particularly the description of the normal aging personality, the discussion of the dependent needs

of older people, and Mr. Tibbitt's discussion of some of the things that older people need to be able to do.

This interests me insofar as it applies to some of the mechanisms that may be at work when older people become mentally ill. Certainly, over a variable period of years, depending upon constitution, heredity, and environmental factors, impairment occurs in the physical and mental condition of aging people. This impairment, at our present stage of knowledge, is inevitable. What could happen, if we were able to use generally, even now, what is known about metabolism and how it may be influenced in older people?

The newer knowledge is not in general use. There is nothing miraculous about it. Many things have to be discovered in the application of some of these principles in general medicine. What effect they may have will not be known for a number of years.

As physicians and psychiatrists, we are interested in keeping our aged people in the best possible state of health. That is to say, that we know how susceptible aging people are to stress of various kinds. We cannot always distinguish between a person's dependent needs and his needs with reference to his outside environment. They both exist, and how he responds is of great importance.

We know that homeostatic mechanisms in the older person operate on a very narrow margin. We are quite accustomed to knowing and observing that certain things may happen to the elderly person who is coasting along very well. He may have a slight memory defect; he may have transient periods of confusion. He may even have had a hemiplegia; he may have had all kinds of organic disease.

We know that, nevertheless, he may become fairly well adapted—sometimes exceedingly well—until something happens that upsets his equilibrium. Then a mental illness develops. So, the things that have been mentioned interest me because of the absence of fulfillment of some of these needs. Something that disturbs the older patient may upset his delicate, or at least impaired equilibrium and cause a mental illness. In 1940, we studied 100 patients with psychosis with cerebral arteriosclerosis at the New York Hospital, Westchester Division, in White Plains. There were certain very striking facts about that group of people; one concerned the causes of their sickness.

We think, when a psychosis develops in an older person with cerebral arteriosclerosis, senile psychosis, or some other condition, that he has had a progression in senile changes or arteriosclerosis which may have accounted for the upset. However, that does not usually seem to be the case. It is rather that the person has undergone some stress. This is not always a physical stress, because we found in these 100 patients with psychosis with cerebral arteriosclerosis—they were all psychotic patients and very sick—that emotional causes for the upset were conspicuous in 76 patients.

The emotional changes varied in all kinds of ways, depending upon the person. Many of the complaints were quite common; *e.g.*, in several cases there had been a death in the family. Some loved one was lost, and the patient's identification with, and dependence upon that person were interrupted. Not

infrequently, for an older person who had lived in the community for a long time, just the question of having to move away from home to some place unknown and strange was enough to precipitate confusion. A memory defect was obvious—sometimes delirium. So, emotional aspects of mental illness in the aging are readily apparent.

Of this group of 100 persons with psychosis with cerebral arteriosclerosis, 11 recovered and 2 or 3 continued to work. One, who was 85 years of age, continued to go into the office for quite a long time after his illness. Forty-nine were able to go home. In addition to the 11 who recovered, 12 were much improved and able to get along well at home, whereas 26 others did less well at home.

This study showed the importance of emotional causes in older people suffering from mental illness. In 1950, we reviewed the records of 365 patients past the age of 60 years admitted consecutively to the New York Hospital, Westchester Division, and described the results in a paper entitled "The Outlook for Patients Admitted to a Mental Hospital After the Age of 60."

The admissions of the 365 older persons occurred over a period of years, because we do not devote our sources primarily to older people, but to younger people who have been considered to be recoverable. Perhaps 10 per cent of our patients are in the older age group.

About 60 per cent of the 365 had functional illnesses. The course of their functional illnesses was much the same as in younger people. A large percentage of them recovered. Many who had organic disturbances recovered. Here again, many of the precipitating causes of mental illness were noted to be deprivations, changes, losses, and the like.

All of this resolves itself into a very interesting problem, because it is a social as well as a medical one.

If mental illnesses are a response to such conditions, it behooves us to see that the lot of the older person is such that he will be able to maintain independence and comfort, and the chance to be creative that Mr. Tibbitts mentioned, with the expectation that many of these illnesses, both functional and organic, can be prevented or delayed.

Methods by which to study the adaptability of an older person and his ability to get well are important. We have recently been carrying out work on some of the prognostic features, and their value in illness in older people. The study concerns the correlation of such things as mental status, organic changes in functioning as shown by the Rorschach test, and the electroencephalogram, and noting the factors that seem to be most predominant in the patients' recovery.

A favorable prediction can be made if the mental status, the electroencephalogram (EEG), the Rorschach test and the neurologic examination all yield negative findings, as in many of the patients with functional disturbances who recovered.

The Rorschach test provides a good index of organicity. During the course of the illness, we would sometimes see improvement in the results of this test as the patient improved. Thus bad Rorschach results were not necessarily a poor prognostic sign. The EEG in 3 or 4 of our functionally disturbed patients

was abnormal. They all recovered, even though the EEG abnormalities persisted.

A study of the effects of the opportunities that an aged person has to live in his community, to express himself, and so forth, in relation to his ability to stay well, is important medically and socially.

MODERATOR ALLEN: Thank you, Dr. Clow. I want to interject a brief material note into the discussion at this point and refer to electric shock and to reserpine and chlorpromazine. If we relate our experiences with cases, we are apt to have subjective impressions about those conditions. Of course, the impressions vary a great deal and we are perhaps apt to be enthusiastic about certain cases in which we have apparently helped, and to be a bit pessimistic and reticent about those in which the results have not been so favorable. We have some facts that we ascertained at the New York Hospital, Westchester Division, first, with regard to electric shock therapy in relation to involutional melancholia.

With the use of electric shock, the whole picture of involutionary melancholia has changed. We no longer see marked delusional and hallucinatory formation because we see the patients relatively early and abort these symptoms. In the old days, McCurdy gave an interesting description of involutional melancholia in his *Psychology of Emotions*, a valuable book which I believe now is out of print. He stated that involutional melancholia generally starts with features somewhat similar to most neuroses and then the patients become depressed. They develop delusions or beliefs as to approaching torture and death, or delusions that have to do with bodily change and disease.

We rarely see these symptoms now. We generally find patients treated with electric shock entering a stage of mild depression, being somewhat agitated, being restless, but not having full-blown delusions.

With the use of electric shock, we have also shortened their length of stay in the hospital from an average of two years to approximately eight months. With the various electrotherapies and chemotherapies, a definite advance is being made.

With the administration of chlorpromazine and reserpine, we are able to use even less electric shock therapy than before.

From April to July 1954, on the male service of our hospital, 6 patients were treated daily by electric shock. With the advent of treatment with chlorpromazine and reserpine, we found that over a comparable period in the following year—April to July 1955—the number of patients treated by electric shock had been reduced to 3+.

During June 1955, no electric shock therapy was given during one ten-day period. It can be readily inferred this was probably because of the type of patients we had at the time. At any rate, it was the first time since we started electric shock therapy that we were able to go for such a long period without having to use it. Throughout our hospital, the number of treatments needed has been somewhat reduced. We sometimes continue electric shock for a time and then give the patients chlorpromazine or reserpine. Sometimes we do not need to resort to electric shock therapy again. We are generally conservative,

but when administering the tranquilizing drugs we use doses of 2 to 10 mg. of reserpine or 40 to 400 mg. of chlorpromazine daily. Larger doses can be used. A patient recently came to us who was receiving a dosage of 900 mg. of chlorpromazine daily, and who showed definite parkinsonian symptoms.

This, roughly, has been our experience, and these are the conclusions at which we arrived.

I should like to ask at this point, Dr. Offenkrantz, what your experience has been at Creedmoor. Have you anything to offer regarding treatment of the aging?

DR. OFFENKRANTZ: We have had rather brief experience with chlorpromazine and reserpine in a variety of conditions, and find them extremely useful drugs.

From the standpoint of psychiatric research, we are still somewhere in the Dark Ages. It behooves those of us who wish to identify ourselves with research organizations in psychiatry to see what can be done through an inter-disciplinary approach to the problems of understanding human maladaptive behavior.

For example, the problem of introducing drug molecules, one way or another, into patients in the aging period who are maladapted to the extent that they are hospitalized in a State Hospital in the New York State Department of Mental Hygiene, has been the focus of our geriatric research in recent months.

In a primitive way, we have been trying to use the various disciplines that are in operation at Creedmoor Institute for Psychobiologic Studies in a therapy evaluation project. We were interested in determining whether or not we could evolve a respectable scientific methodology for studying the patients. The disciplines participating were clinical psychiatry, neurology, psychology, physiology, nursing, and biochemistry. The particular molecule under consideration was not particularly important, but it was reported to be, as are many drugs, unusually effective in the treatment of varying conditions of the aging period including senile dementia with or without arteriosclerosis. It happened to be an extract of a fatty acid derived from carp, which is an extremely long-lived fish. In a "double blind" study we found that the drug, which had been highly effective in the hands of honest investigators dealing with problems of the aged on an out-patient basis, had no effect on the patients in our studies; nor was any placebo effect obtained. We believe we are in an unusually advantageous position from an experimental standpoint in state hospitals such as Creedmoor, because we have aged patients with little motivation to get well. These are people who often have no families, or rejecting families. We have, in effect, a kind of standardized experimental situation, in that these people would have nowhere to go, were they to improve.

Furthermore, it is important for those who are interested in administering drugs which act primarily in the central nervous system, to be cautious when dealing with the disorders of the aging period; simply because of the dangers inherent in putting a 12-cylinder engine into a Model T chassis. If the drug works, one should be prepared to help such a patient determine where he is going and what he will do.

I should like to make a final point. I accept Mr. Tibbitts' criticism as a valid

one concerning my comments to general practitioners about ways of getting along with geriatric patients in order to help them. I agree with him. It is a problem for, and a function of, the society in which we live to provide the means by which an aging individual can function. However, this is not something that in most instances can be handled by either a general practitioner or a psychiatrist. I feel Mr. Tibbitts' remarks in this respect were directed to all of us, not as practitioners of general medicine or psychiatry, but as citizens of the community in which we live with the aged population.

MR. TIBBITTS: I did not mean to be critical, Dr. Offenkrantz. I wanted it to be recognized that the whole job does not lie with the physician, that others in society were involved, too.

MODERATOR ALLEN: Are there any questions? I have some with regard to insomnia and depression that I am going to give to Dr. Clow.

DR. CLOW: The first question is: How do you prefer to treat the depression which so often accompanies old age?

Depression does not occur out of context. First, we are interested, if possible, to find out why a patient is depressed. It may be, and often is, because of some situational difficulty. If so, we try to talk to the patient, and perhaps to his family, to see whether anything can be done. There often can be, because people at this age may become depressed in response to deprivations of various kinds.

Suppose a patient is very depressed and is a suicidal risk. If he is otherwise in satisfactory health, we would probably think of electric shock treatment; that is, if the depression is psychotic and the patient is able to take it. Most of them are. Electric shock treatment is contraindicated in very few.

The second question is: Is shock therapy safe, and up to what age, when there is cardiovascular disease with hypertension?

We cannot say arbitrarily up to what age electric shock treatment will be safe, but if the patient is in fairly good physical health, he can be treated. Cardiovascular disease with hypertension is not necessarily a contraindication to the use of electric shock. Common sense must be the guide, but the chief contraindications to electric shock treatment are the presence of a recent myocardial infarction, possibly auricular fibrillation, or some disturbance in the rhythm of the heart that might become ventricular fibrillation. If the heart is fibrillating, quinidine should be administered, if possible. We have treated people up to 80 years and even older with electric shock, haven't we Dr. Allen?

MODERATOR ALLEN: Yes, in the eighties.

DR. CLOW: You do have to take into consideration the fact that some older people have osteoporosis, and in such cases a curare product would be a suitable thing to give.

DR. OFFENKRANTZ: The first question is: Please give the full name of Rosenthal, the title of her paper, and the publisher.

The title of Dr. Pauline Rosenthal's paper is "Second Childhood," *Geriatrics* **10:** 382–390 (Aug.) 1955.

The next question is: What does Dr. Wilson mean by humoral control in the individual undergoing the aging process?

I do not know what Dr. Wilson means by that. I presume it is a general

reference to the endocrine system, but to which factors in it I am not able to tell you, beyond the familiar observations relating to the decrease in testicular and ovarian function.

However, it may be of interest that in our investigation of the known cases of progeria, *i.e.*, premature physiologic aging occurring in infancy and childhood, lesions in the hypothalamus were apparently related to the disease process.

The third question is: Please define free-floating anxiety. May I refer this to the panelist who used the phrase.

DR. DANIELS: Dr. Allen used it.

MODERATOR ALLEN: That is an excellent question. All of us have a free-floating anxiety. It is something which we long to attach. What becomes free-floating anxiety is something that is dissociated from the original etiologic factor. We become unaware of what the etiologic factor was, and then somewhat as in a fixation reaction, we seek for something to which to attach the anxiety. Sometimes this results in kleptomania, the commission of crimes, or sometimes even murder. The individual seeks something to be anxious about.

If anyone else on the panel has a better explanation, I shall be glad to have him offer it.

DR. CLOW: One of the nasty things about it is that when the person is cured of a particular anxiety it "free-floats" to something else. The patient is then worried about something else, which indicates that the anxiety is the main thing. The thing to which it happens to be attached at a certain time isn't quite so important. You relieve the anxiety about one thing, and the anxiety floats or moves to something else.

MODERATOR ALLEN: One more question I should like to answer is from Dr. Friedman: What do the members of the panel think of re-evaluating the subject of senility? This is becoming an ever-increasing problem in the economic, sociologic, and medical fields. He believes there is such a thing as a happy senile patient—simple deterioration without frank psychotic manifestations lost in the larger classification of senility.

We do have a classification of psychosis without senility. I have several such patients. I have one now that I have treated for psychoneurosis—a man in his eighties—but he is not psychotic. The other day someone said that he was having trouble at home, he can't get along with his wife and son, and he ought to be sent to a state hospital. The point is that he was the most alert and active person in the home. The son had been a cretin and was mentally deficient. His wife was beginning to show changes of senility, and she was the one who really ought to have been sent to an institution.

I think a rather happy phrase is senescence without psychosis.

DR. OFFENKRANTZ: I have a loaded question to answer, but one which I think is a good one.

If the physician is not equipped alone to deal with the emotional needs of older adults, should he turn to the social worker for assistance and form a team in order to help the patient?

Certainly. I would say, however, not to turn to the social worker alone, be-

cause there may not happen to be such a person available to the physician. I believe it is dangerous for a physician to think that a particular discipline has certain things to offer and that no one else can offer anything similar to it.

The judicious employment of any assistance in the life of the patient—the family, the friends, the employer, as well as the physician's office nurse—is also appropriate. Social workers, however, by virtue of training and experience are uniquely equipped to help a physician handle this type of problem.

DR. CLOW: The next question is: Are sex hormone combinations useful in preserving mental capacity or tone in the aging?

That question has probably never had an absolute answer. Because of a general beneficial effect that hormones seem to have and because of the thought that there is some diminution in secretion of these hormones in old people, there has been a tendency in the last few years to think that they might be helpful.

I have in mind a communication from the Worcester State Hospital with regard to a project that they are undertaking with the use of hormones, which happens to be in relation to the alpha-ketosteroids. They have given a certain number of older people enough of the ketosteroids to bring the urinary excretion level to that found in a younger person. So far, these patients have showed no change in tests of mental capacity and memory, but they have showed an increase in muscle power.

Apparently, there is some indirect benefit. Certainly, some older people do seem to be better after receiving hormones. Whether it is because of the hormones, or because of the suggestive effect, is not clear. The matter requires much more elucidation before we can be certain about it.

MODERATOR ALLEN: Our time is up. For myself and for the panel, I want to thank Dr. Henderson for the privilege of participating in this interesting symposium.

CHAIRMAN HENDERSON: I should like to offer my thanks, as President of the American Geriatrics Society, to all of the members of the faculty who took part in this symposium, and especially to this group of experts who have given us such a wonderful discussion on one of the really major problems of our time.

When you consider that more than 52 per cent of all hospital beds are occupied by patients with mental disease, both young and old, you can realize that there is really a problem.

PROBLEMS ASSOCIATED WITH THE INCREASING RATIO OF MALE OVER FEMALE MORTALITY

WILSON T. SOWDER, M.D.* AND JAMES O. BOND, M.D.†

Jacksonville, Florida

For several years one of the authors has been calling attention, by articles and other means, to the striking increase in the difference between the mortality rates of males and females in recent decades. Some interest has been shown in the subject, although there have been other reactions which have ranged from indifference to levity and from skepticism to the amused toleration received by a person who is normal in all respects except one. Talks on the subject have been publicized as humorous and the facts presented have been discounted with the charitable attitude that exaggeration is permissible when the subject is not important, and serious acceptance not expected.

The author of these original papers (1, 2) has at times felt like a child who sees a bear, but whose parents tell him it couldn't possibly be a bear but must have been a dog. Parents can be very persuasive in such situations, but if the bear doesn't go away the child's opinion may eventually prevail. Since the first articles on this subject were written, it has become more and more evident that the gap between male and female mortality rates is steadily widening and the authors take courage from these facts to call attention to some of their implications.

MORTALITY DATA

Methods

Table 1 lists the basic data. It shows that, although the mortality for both sexes is declining, the mortality for females has declined much faster during the past three decades. Table 2 shows the percentile excess of white male over female death rates, by age groups, for each of the decennial years 1900 through 1950. These excesses have been steadily rising for each age group throughout this period, and the ratio of male over female death rates is highest at ages 15–24 and 45–64 years.

Another way of studying this problem is to examine the data by an approximation of the cohort or generation method. In this method each cohort is followed and the ratios of male to female death rates are recorded by age while that same group of people move through their life span. For example, the cohort born in 1865–74 can be followed from the year 1900, when they were 25 to 34 years of age, across the diagonal outlined in Table 2 until they were 75–84 years old in 1950. The percentile excess of male over female mortality as the successive generations went through life is shown in Table 3 and Figure 1.

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TABLE 1

Age-Adjusted Death Rates by Race and Sex for the United States and Florida—Selected Years

Year	Age-adjusted Death Rates per 1,000 Population				Percentile Excess of Male Rate over Female Rate	
	White males	White females	Non-white males	Non-white females	White	Non-white
United States						
1900	18.4	16.8	28.7	27.1	10	6
1910	16.7	14.4	24.8	23.2	16	7
1920	14.2	13.1	20.4	21.0	8	−3
1930	12.8	10.6	21.0	19.2	21	9
1940	11.6	8.8	17.6	15.0	32	17
1950	9.6	6.5	13.6	11.0	48	24
1953	9.5	6.1	13.2	10.2	56	29
Florida						
1920	13.8	12.1	19.5	18.8	14	4
1930	13.1	9.8	23.3	19.5	34	19
1940	11.5	7.5	20.1	15.8	53	27
1950	9.1	5.6	14.7	11.0	62	34

Total United States population of 1940 used as standard.

TABLE 2

Percentile Excess of Male Over Female (White) Death Rates, By Age Groups, by Decennial Years, United States, 1900–1950

All Ages	Year					
	1900	1910	1920	1930	1940	1950
Less than 1	23.6	24.1	29	27.7	30	32
1–4	8.0	9.2	9.0	14.5	16.7	27.0
5–14	0	7.1	17.0	28.6	37.0	40.0
15–24	3.5	14.5	−2	20.0	43.0	114
25–34	**0**	13.5	−9	13.9	27.0	64
35–44	10.4	**26**	5	26	38	58
45–54	10.7	27	**10**	34.8	52	78
55–64	11.7	21.4	12	**28**	50	78
65–74	10.7	12.2	9	19.8	**30**	50
75–84	7.8	8.3	5	11.8	15.7	**24**

This method assists in differentiating between the effects that age alone may produce in susceptibility or predisposition to a given phenomenom and the effects related to the time-periods in which the different generations lived (3).

Interpretation

Because of the short period of time these cohorts were followed, any conclusions drawn must be considered tentative. From our examination of the data, we note that the apparent selection of ages 15–24 and 45–64 for excess male over female mortality (Figure 2 and Table 2) disappears in the cohort graphs. Rather, there is a steady rise of M/F ratios as each generation goes through

TABLE 3

Percentile Excess of Male Over Female (White) Death Rates Per 1,000, By Cohorts, By Age

Cohort Birth Years	Age							
	5–14	15–24	25–34	35–44	45–54	55–64	65–74	75–84
1815–24								7.8
1825–34							10.7	8.3
1835–44						11.7	12.2	5
1845–54					10.7	21.4	9	11.8
1855–64				10.4	27	12	19.8	15.7
1865–74			0	26	10	28	30	24
1875–84		3.5	13.5	5	34.8	50	50	
1885–94	0	14.5	−9	26	52	78		
1895–04	7.1	−2	13.9	38	78			
1905–14	17	20	27	58				
1915–24	28.6	43	64					
1925–34	37	114						
1935–44	40							

life. Moreover, as the generations occur later and later in time, this rise is progressively steeper, and the excess begins increasingly at younger ages.

We interpret these observations as showing that age alone (*e.g.*, ages 15–24 or 45–64) is not the significant factor in excess male over female death rates. Rather, the point in time when the generations were born plays the important role. The later in time they were born, during the past hundred years, the more selectively they were affected.

Since the older generations born before the period 1875–1900 showed no marked rise in excess male over female death rates, as they passed through the period 1900–1950, it could be postulated they were born too soon to be influenced by the factors which have caused the striking increase in excesses since 1900. Similarly, the generations born after 1875 would seem to have been particularly affected, and obviously the influence was exerted during their younger years. So far as the authors know, no biologic changes have occurred that would have selectively affected mortality by sex during this time. However, marked cultural changes have taken place during this period. The hypothesis that these have in some way influenced the mortality of the sexes differently is apparently supported by these observations that older people born and reared in a different cultural milieu, have remained relatively unaffected. Other explanations may be equally plausible, and it is the major purpose of this article not so much to prove a theory, as to stimulate further inquiries into the reasons behind this remarkable phenomenon.

It has been previously pointed out that a higher male mortality occurs from almost every major cause of death which is not sex-specific, and furthermore that some of the major causes of death of females (such as diabetes, and cancer of the uterine cervix and breast) are particularly amenable to early treatment. This fact, when contrasted with the difficulties in the successful treatment of some of the diseases from which males more often die (such as cardiovascular

PERCENTILE EXCESS OF MALE DEATH RATES OVER FEMALE, BY AGE AND BY COHORTS (UNITED STATES, WHITES)

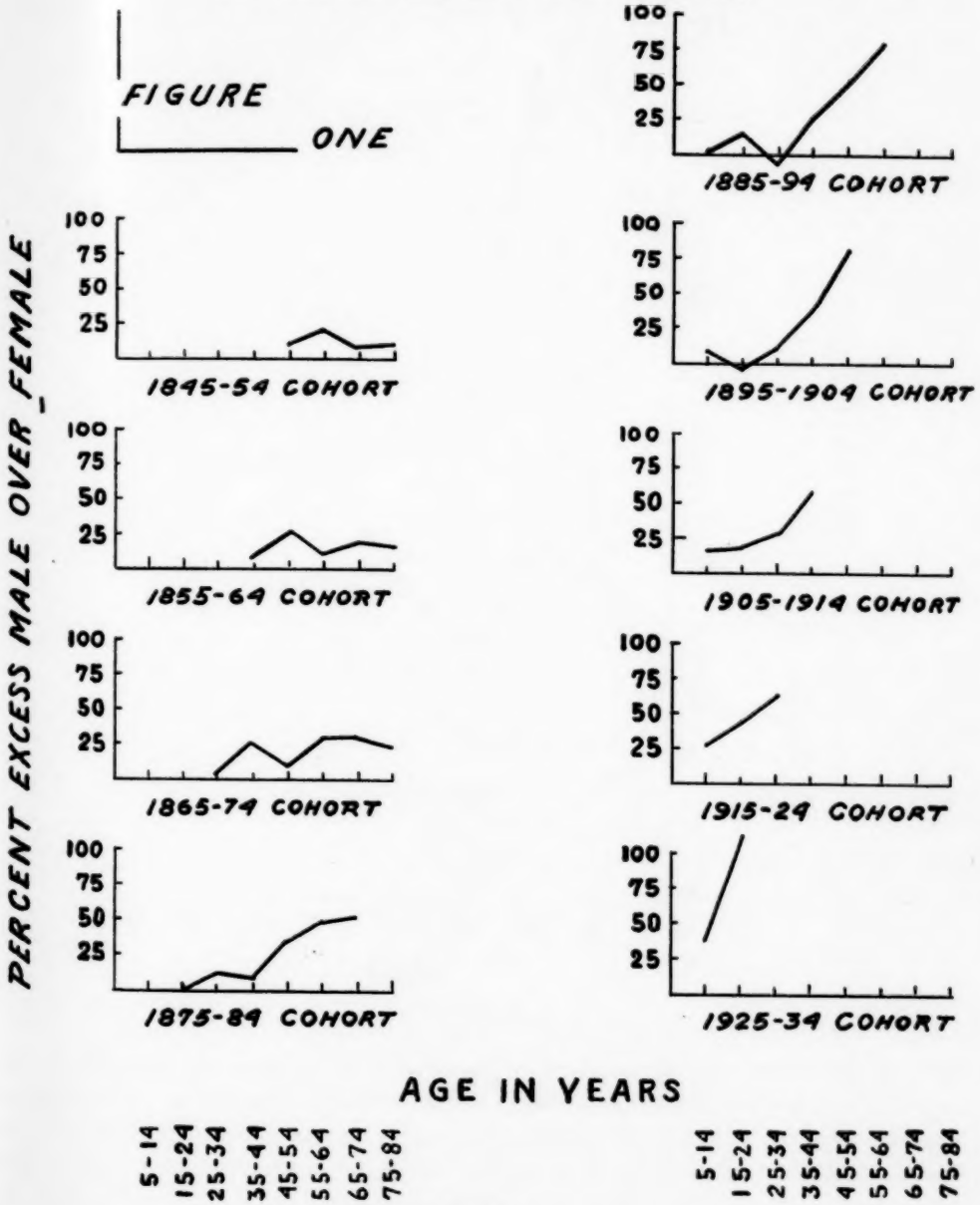

FIGURE 1

renal disorders, and cancer of the lungs, stomach and duodenum) portends an even greater difference between the mortality rates of the two sexes in the future.

Walter G. Bowerman of the New York Life Insurance Company has also called attention to the same phenomenon (4) and has presented some very interesting figures on the subject. Figure 2 shows clearly the tremendous rela-

PERCENTILE EXCESS OF MALE DEATH RATES OVER FEMALE, BY AGE (UNITED STATES, WHITES), FOR YEARS STATED

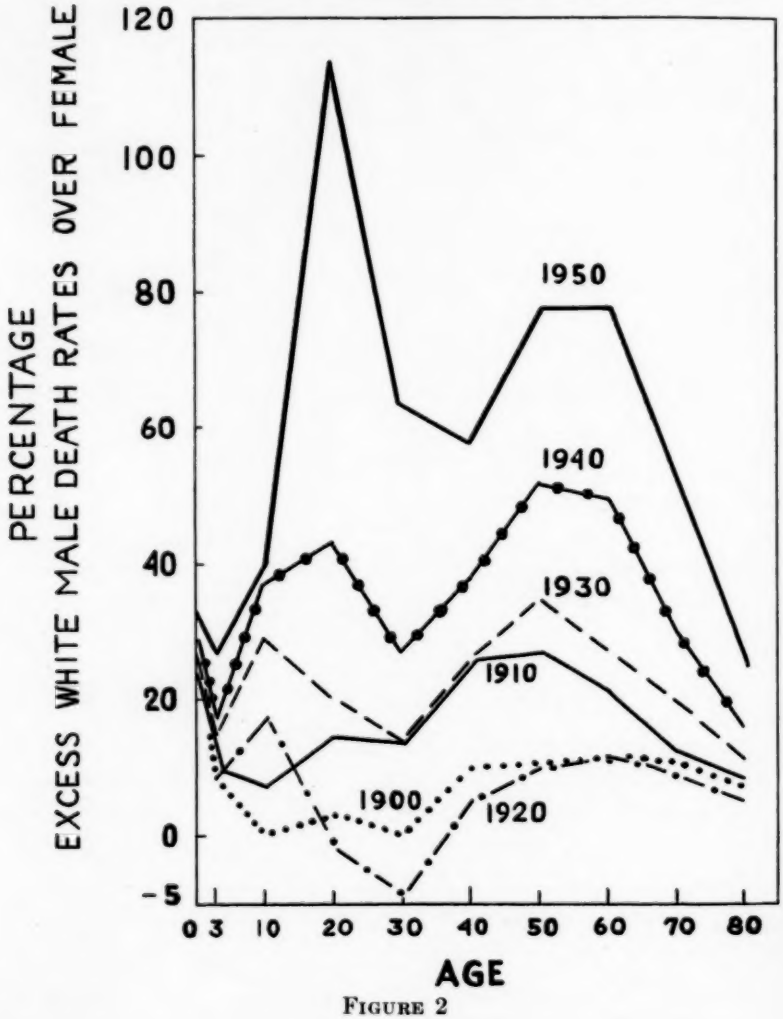

FIGURE 2

tive change that has taken place in the relationship between male and female mortality rates since the beginning of the century. Bowerman is inclined, as are the writers, to ascribe the higher mortality of males in later childhood and early adult life to greater environmental hazards, and particularly to accidents. He suspects, as do the writers, that cultural changes have much to do with the higher mortality of males in later life and especially up to age 65. The writers strongly endorse his suspicion that "Women have perhaps adapted themselves better than have men to the atomization, nationalization, and artificialities of modern life." Bowerman also notes the lack of awareness of the problem. "Probably very few actuaries or biostatisticians have observed the marked differences in recent mortality rates, when set forth for each sex." He says that when he showed some of his figures to the head of the astronomy department of a great

university he "reacted like the farmer who saw the giraffe for the first time, saying 'I just don't believe it.' " Bowerman shows why there can be a considerable difference between the mortality rates of the two sexes and yet the numbers of the sexes remain approximately the same for many years. As is well known, more males are born than females, or about 106 of the former to each 100 of the latter. Even though there are substantial differences in the mortality rates of the two sexes up to the middle life the actual mortality for both sexes is low.

The Statistical Bulletin of the Metropolitan Life Insurance Company has pointed out (5) that before 1930 more men than women migrated to the United States, and since that time there have been more women among our immigrants. Also, it was pointed out that more men than women emigrate from the United States. The widening difference in mortality rates between the sexes, and the foregoing facts with respect to migration plus war deaths, were bound eventually to bring about a preponderance of females in the population of the United States, in spite of the birth of 6 per cent more males. This has occurred and was shown for the first time in the Census of 1950, when females outnumbered males by 1 per cent. Although it has taken many decades for all these factors to produce a preponderance of women, and a national census to certify the fact, the time is drawing near when it will be evident to everyone. The Statistical Bulletin of the Metropolitan Life Insurance Company in an article (6) on future population trends predicts that by 1975 females will out-number males by nearly 4 per cent in the entire population—in the 45–64 age group by 11 per cent, and in the 65-and-over age group by nearly 40 per cent (Table 4). Even in 1950 at ages 65 and over, females were in the majority by nearly 12 per cent. This change in the make-up of our population is having, and will have, greater repercussions in many aspects of our society. It means that a greater percentage of our older people will be women. It means more widows and longer periods of widowhood. Unless the practices and patterns of employment change, it means a greater proportion of our population will be unemployed and unemployable. Insurance companies may recognize this trend by charging men more and women less for life insurance, and by the reverse in case of annuities. If the

TABLE 4

*Population of the United States, 1950–1975.—Females Per 100 Males**

Year	Age					
	All ages	Under 5*	5–19*	20–44	45–64	65 and over
1950	101.0	96.2	97.2	103.1	99.8	111.6
1955	101.6	96.1	96.3	102.8	103.4	116.0
1960	102.2	96.0	96.0	102.1	106.5	121.8
1965	102.7	96.0	95.8	101.1	108.6	128.0
1970	102.9	95.9	95.7	99.8	110.1	133.4
1975	103.9	95.8	95.7	98.9	110.8	137.8

* Reproduced by permission of the Metropolitan Life Insurance Company.

struggle of making a living and providing for the welfare of a surviving widow has anything to do with the earlier death of men, the prospect is that he will have to struggle harder in order to provide for the lengthening life of womenfolk, and as a consequence will shorten still further his life span as compared to that of his mate. This may seem to be a gloomy outlook but at the present time it seems to be a reasonable prediction. It is a matter of opinion whether the outlook for men is brighter than that for women. Certainly widowhood, loneliness, and reduced financial circumstances are difficult for persons of either sex, and adjustments to such changes and situations are not made easier by age nor by the fact that they are commonplace.

There is an urgent need for a more general recognition of the fact that the higher mortality of men is steadily decreasing the proportion of men in the population; and that biologic, psychologic, social and economic problems are bound to follow.

SUMMARY

The growing importance of the relative excess male over female mortality in the United States has been presented. The effects of this difference will become increasingly apparent in the older age groups, in which the factors producing an excess of females in the population reach their final culmination.

The possible factors operating to produce this excess are discussed, but it is pointed out that they are not accurately identified. The need for further research to accomplish this identification is emphasized by the social, medical and emotional problems that the excess older female population will present, as well as the problem to the home and the nation of the premature loss of male lives.

Acknowledgments

The authors gratefully wish to acknowledge the assistance of Dr. W. P. Shepherd of the Metropolitan Life Insurance Company, who granted permission to use some of their statistical data; and of Mr. Everett Williams, Director, Bureau of Vital Statistics, Florida State Board of Health, who kindly reviewed the statistical material presented in this manuscript.

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DISCUSSION ON PALLIATION IN CANCER*

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Dr. C. J. Gavey:

In patients with inoperable cancer we are not necessarily dealing with hopeless cases, for hope must remain, but nevertheless the problem is usually that of the management of the individual who is nearing, or who has actually reached, the terminal stage of life.

Pain.—The first great principle concerns the relief of pain when it is present. Patients have a right to know that we really can relieve pain. Once assured of this, they can take a more philosophical view of their disease for it is difficult to be philosophical when in pain. A recent survey of public opinion on cancer by Paterson and Aitken-Swan (1954) shows quite clearly how alarming the thought of cancer usually is. The women interviewed rated cancer as the most alarming of the serious diseases and gave the reason why in terms relating chiefly to pain. A victim of cancer may say "I am not afraid of death but I am afraid of pain and I suppose I am bound to get worse" (Clark-Kennedy, 1954). Patients who have recovered from cancer describe their emotions in an almost uniform manner. They have dreaded pain and found it to be far less than they had anticipated. Indeed some have expressed the idea that the medical profession should make a special point of dispelling the prevalent impression that cancer is necessarily very painful.

Assessment of the degree of pain comes fairly readily to those with experience but newly qualified doctors and inexperienced nurses often go wrong on this point. The bias is not enough in favour of the patient. Indeed, how can we judge the intensity of pain? In the one patient a given lesion may cause exquisite pain, in the other the same lesion is better tolerated. Thought given to this simple problem leads me to recommend that if there is substantial pain it is wise to give an analgesic continuously and to add whatever else is necessary from time to time. Too often one finds a patient who has gone without an analgesic because he has not complained of pain at the opportune moment. I know of nothing better for continuous analgesia than Mist. Acidi Acetylsalicylici Opiata, four-hourly [Tinct. of opium 8 minims, Aspirin mixture (B.P.C.) to ½ fl. oz.]. A few cannot tolerate aspirin, in which case codeine can be given instead.

Another point of importance is the too rigid avoidance of drugs of addiction. I refer particularly to pethidine (100 mg. = 16 mg. of morphine). Addiction is, in fact, uncommon, too uncommon to weigh at all in the decision whether or not it should be used. Pethidine has advantages over morphine in that it does not

* This discussion took place at the meeting of the Section of Surgery, of the Royal Society of Medicine held in London, England on January 5, 1955, and was published in the Proceedings of the Royal Society of Medicine, Volume 48, page 703, 1955.

To Doctor J. M. Browne-Kutschbach, Editor of the Proceedings of the Royal Society of Medicine, and to each of the participants in the discussion the Editors of this Journal wish to express their sincere thanks for permission to reproduce this article.

cause mental lethargy in those who do not wish to be "doped" in the mental sense, and there are not a few of such patients. Pethidine unfortunately has only a brief action, lasting two to four hours. Methadone (10 mg. = 10 mg. of morphine) is also valuable but its depression of cough may lead to trouble in emphysematous or old patients and bad dreams are sometimes a nuisance. Phenadoxone (10–30 mg.) has an analgesic effect for three to four hours when given by mouth and it also possesses a mild sedative action. Hypnotics such as sodium amytal and hexobarbitone are effective provided they are repeated without hesitation, and are used with analgesics. Chlorpromazine has proved its worth in patients with intractable vomiting. Given by mouth the drug may be retained long enough to be absorbed, but if it is rejected, parenteral administration is available. The dose is 25–50 mg. t.d.s. If we do not want mental sedation it should be stopped when vomiting ceases but we need not fear the more serious side effects such as liver damage in these patients. R 48 is in my experience really useful in reducing pain from hepatic secondaries.

In the terminal stages, morphine is, of course, still the most valuable drug and it should not be spared when the time has come to use it; but when that time shall have come is often hard to decide. When observing patients with inoperable cancer, we can detect perhaps more clearly than in any other fatal disease, a fairly sudden change, from one day to the other; a change in both physical state and outlook arising from overwhelming weakness; a sign that the body has given up the struggle. From this point morphine should seldom be withheld and considerable pain will determine its earlier use. It is wise not to exceed single doses of 20 mg. of morphine; repeat it if necessary after a suitable interval. Hyperduric morphine mucate, 16 mg., lasts longer and when combined with hyoscine mucate it is especially helpful in relieving tracheal rattle.

When there is no pain in terminal illness, morphine should not be used automatically but it has a limited place. I have not used cocaine but some physicians think highly of it in these circumstances. The decision as to when, if ever, the patient should be helped over the border, rests on a higher plane of judgment than can be laid down in rules or laws and it is for each practitioner to decide for himself carefully how far he can assist his desperate patient without transgressing the law (Gavey, 1952).

Telling the patient.—We have gone a long way since the days of Paget (1814–1899) who accepted a contest in brevity with a patient who came into his consulting room and merely thrust out his lip saying "What's that?" "That's cancer," he answered. "And what's to be done with it?" "Cut it out!" said Sir James. I do not suggest that there is often difficulty in telling patients what is necessary but a minority in whom it is difficult may be reduced if we bear in mind that patients do not share our knowledge of the terminal stage of disease. Occasionally the patient seeks such information. "What will be the manner of my going?" he asks. Few realize "how easy it is to die" (William Hunter). Few realize the clouding effect of the "toxæmia" that ends in death.

When patients persistently seek information we must be ready to enlighten them. To refuse to do so may be expeditious but morally wrong unless we are dealing with patients from areas, still to be found here and there in the British

Isles, where the mere mention of cancer, in whatever form, engenders a dread which deters them even from investigation in hospital. The capacity to receive bad news is variable indeed but a nervous disposition alone does not preclude remarkable courage in the face of a grave diagnosis. Sir Frederick Treves (1923) who wrote much on these matters said: "Very often the message can be worded in so illusive a manner as to plant merely a germ of doubt in the mind, which germ may slowly and almost painlessly grow into realization of the truth." Frequent visiting does give an opportunity for that germ to grow and often doctor and patient realize at the same moment that the time has come for doubts to be resolved and a calm ensues which leads to mutual consolation. I think myself that it is best for both husband and wife to know the situation but one's prime obligation is to the patient's wishes in the matter. Dean Inge's (1939) view was: "On the whole I think the patient has a right to know the truth."

The power of self-deception may be very great and it behoves us to promote this at times; otherwise the patient may become intolerable to himself and to his family. Self-deception may arise from the patient's realization of his incapacity to receive decisive information. However, most patients can accept the truth slowly if we attend to proper preparation for it, and when imparting the truth we can still stress favourable features which are usually not hard to find, at least in regard to the immediate prognosis. It has been said of a certain surgeon that when he told a patient of cancer in his own inimitable way the patient found it an acceptable illness.

I feel that there is no place for a deliberate lie, or for silence. A priest once told me that "a considerable number of patients say that doctors tell them nothing, or practically nothing, about their complaints. Not a word of explanation or sympathy or hope and the poor sufferers are left with their guesses wondering what is going to happen next". The priest was fully aware of the reasons for reticence but had no doubt that it was often too severe.

Intelligent patients, now better informed in matters medical, present us with ethical problems increasingly similar to those arising in medical men or nurses who fall victim to cancer. In these circumstances there is more room for frankness, if it is sought. That is the determining factor though we must allow the patient opportunities and be ready with suitable answers. It is difficult, well-nigh impossible, to continue visiting such patients if they do not have a reasonable idea of the truth. Some of the finest examples of resignation and serenity have occurred in medical men.

For completeness I mention the patient who never suspects that the end is near even though one has acted on the supposition that he did know, and who speaks of recovery and of holidays during the next year. Near relatives have assured me that such a patient, intelligent enough, had no suspicion whatsoever of death even on the last day. I should say that when I have allowed this to happen, the near relative's desire that the patient should not be told (because of incapacity, real or otherwise, to receive the truth) has influenced me in not volunteering the information. I realize that Roman Catholics would condemn this attitude, and it would not arise concerning a patient of that faith.

Visiting.—I do not profess to have complete insight into what the patient feels

when he knows he has an inoperable cancer. The more one studies the question the more baffling it is. We partly overcome the difficulty by using a kindly attitude but it is hard to determine how supportive it really is. It is here that the personality of doctors and nurses comes in. *Frequent visits* are fundamental even if we do nothing overtly and it is for us to take or to seek opportunities of helping in this way. I stress this because modern medicine and surgery enable us so often to spend our time helping in a very concrete and substantial way that we have little time left, it seems, for simple visiting. While recognizing the impossibility of reaching the ideal amount of visiting I do think we should from time to time ask ourselves whether we are paying enough attention to this important aspect of our work. It would be a pity if we should ever deserve the reproof: "the doctor has lost interest in my case." The senior nursing staff feel their task to be infinitely easier if the chief takes adequate time at the bedside of the patient who has almost run his course. In hospital it is very necessary that the patient should know conclusively who is actually in charge of his case. There must never be any room for doubt about this. The risk of such doubt is small in this country compared with some others.

At home a visit may enable a trifling but trying symptom to be quickly removed. The task of relatives is also made easier if the doctor visits regularly and often and he may note in a relative the need for an intermission in nursing before a breakdown occurs. I think there is a good deal to be said for advising relatives to show their sympathy by being practical and by avoiding a hush-hush attitude when the truth is known. We do not want "sympathy" to be the hardest thing the patient has to bear, though I am not suggesting that this is common.

We must not detract from the value of faith which is one of the positive virtues. As Paul White (1951) said: "We need to analyse more than we have yet done the physical effect of the influence of courage, optimism and patience. We have paid perhaps undue attention to the reverse, that is, the harmful effects of fear, sorrow or anger."

Surgery and radiotherapy.—The proper employment of radical surgical measures and radiotherapy calls for the finest judgment. Thus in the relief of pain from bony metastases from carcinoma of the breast, bilateral adrenalectomy is most successful, though its limitations are obvious. When in doubt I am biased in favour of surgical measures which offer some prospect of relief, or laparotomy in appropriate cases to achieve certain knowledge that a growth is, in fact, not operable. But the situation may have to rest as Sainsbury (1906) put it: "Finally should the decision be left to us, as in many, perhaps in most, cases it will be, and we conclude that all things considered, it is wiser to stay the hand than to be active with it then we must have the courage to let it be idle and abide the issue." Radiotherapy in its several forms has a big place in the treatment of inoperable cancer and the work should attract some of our best young men.

Of human understanding.—There is need for a "generality of understanding" (Walshe, 1948) in regard to our patients. There is a growing feeling among them that we never should give up hope; that something can yet be done. This accounts for unexpected requests for further opinions and though this may hurt one at

times, it is a trait in human nature which bears understanding and sympathy even when the patient seeks fields of unorthodox treatment. Unreasonable demands should not surprise us when we consider that red and white roses together are still usually resented in the sick-room and number 13 is still held by many to be unlucky.

I pass for a moment to the understanding of the terminal phase. At this time let us remember that the belief in life after death is almost universal, so it is wise to assure that spiritual help is available. But I agree with Osler and others that it is not incumbent upon us, as medical men, to give it—simply to see that it is available. It is a fact I think that most patients are not afraid of death but they are reluctant to die. In his address on one of my patients who died of carcinoma, the Dean of Westminster said: "The courage and serenity with which she faced the prospect of death was an example to us all. It was a form of courage and serenity which sprang directly from her Christian faith and from her belief in the reality of life to come. Thus she died at peace with God and in sure and certain hope of eternal life."

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Professor Norman M. Dott:

I speak on this subject as a neurological surgeon. Cancer is foreign to neural tissues and is encountered by the neurological surgeon as an invader from other corporeal domains.

The neurological surgeon may be required to deal with cancer in four different ways: 1) he may encounter and deal with metastatic cancer of the brain or spine while the nature of the disease is still in doubt—he then makes the diagnosis and treats the local brain or spinal lesion; 2) when called upon to assist in ameliorating the course of cancer by means of hypophysectomy; 3) when requested to mitigate pain caused by cancer; 4) when required to preserve important neural functions threatened by cancer.

Metastatic cancer of the brain has notably increased in frequency in recent years in proportion to the increase in bronchial carcinoma. In patients over 30 years of age, with rapidly progressive cerebral tumours, radiographic examination of the chest and other appropriate means of search for a possible pulmonary primary neoplasm are routine procedures. Not infrequently, however, the cerebral

metastatic lesion is the first recognizable focus in this disease, and the diagnosis of cancer is first established by exploration of the cerebral metastasis. In these circumstances the neurological surgeon treats the local cerebral lesion with the object of preventing or delaying further cerebral damage. He may proceed to excision of a favourably placed metastasis or to decompression of the less favourably sited or multiple cerebral lesions. Having done so he seeks the help of the oncologist in the management of the neoplasia as a disease entity.

The oncologist is commonly the radiotherapeutic specialist who has the largest experience of neoplasia in its many sites of origin and metastasis and in its various stages of evolution. Not infrequently the oncologist may be represented by a team, with the radiotherapist as leader, supported by a pathologist and an endocrinologist with special interest in the subject. It has become essential for the "system specialist" such as the neurological surgeon, especially when dealing with cancer—a neoplastic disease essentially foreign to his territory—to rely on the oncologist or his team for the management of the disease as a neoplasia.

In the management of cancerous neoplasia it has been found that in the tumours of parasexual origin, especially those of the breast and the prostate, modification of the sex hormone state may profoundly affect the progress of the disease. In the younger age-groups diminution of œstrogens or of androgens by castration, by adrenalectomy or by hypophysectomy has procured striking amelioration of the advancing neoplasia, even in the most advanced cases. In the older age groups the administration of these sex hormones has proved notably beneficial. Whether hypophysectomy has special indications or advantages as contrasted with adrenalectomy or with castration is not yet known. So far as hypophysectomy may be required in the management of neoplasia, the neurological surgeon will join the oncological team to make that contribution.

I think that pain due to cancer could and should be abolished in those cases in which pain constitutes an important factor in the patient's total distress. It is important to recognize that pain has two main aspects—on the sensory level a perception; and on the emotional level a distressful experience. Pain appreciation is a function of consciousness. Modern psycho-physiology, continuing the ancient search for the seat of the soul, visualizes a temple of consciousness with its foundations in the reticular formation of the upper brainstem and in the nuclear masses of the diencephalon and with its upper storeys in the cerebral cortex. In the foundations dwell those shadowy and gigantic forces—the affective functions. In the upper storeys are the more discriminatory or intellectual, but less fundamental functions. The two, working together, constitute the physical mechanism of consciousness. It is believed that the sensory perceptive aspect of pain and its discriminatory sensory accompaniments are functions of the cerebral cortex; while its affective or distressful aspect attains consciousness in the diencephalon.

Pain can be facilitated or augmented by the affective state or tone of the individual—for example when associated with the apprehension occasioned by severe dyspnœa; or with the anxiety occasioned by the increasing enfeeblement from advancing cancer; or again by the anxieties of an endogenous depressive

state. Pain can equally be inhibited by sufficiently potent preoccupation with other matters—for example on the field of battle, at the martyr's stake, and to a lesser extent by religious belief and by philosophical reasoning.

Pain tolerance is also considerably dependent on the time factor. A degree of pain easily borne for seconds or minutes becomes intolerable over periods of days, months or years. Many neural mechanisms are susceptible of fatigue; and the mechanisms of inhibition of pain in cancer are so susceptible. The pain-appreciating mechanisms on the other hand, are peculiarly resistant to fatigue and remain outstandingly acute and unimpaired over long periods. Thus the chronic sufferer—the cancer victim—becomes increasingly vulnerable to pain; his resistance weaker and his appreciation of pain unimpaired and therefore more insistent.

When we survey the chronic cancer victim we see his total distress; and some analysis of it is essential to its proper management. How much is actual pain a factor in his total distress? How much do incidental or endogenous anxieties or revulsions play a part in augmenting such pain as he has or in adding to the sum of his distress independently of pain?

The answers to these questions provide the keys to management. It may be that the methods of psychological medicine, ranging from philosophical discussion and suggestion to electro-convulsive therapy, provide the most effective and sufficient treatment. It may be that analgesic drugs—the simple, acting mainly in diminishing pain perception, the more potent, including the recently introduced chlorpromazine, so modifying consciousness as to blunt distress and suppress anxiety—can provide what is necessary.

Where pain is an outstandingly severe and prominent factor in the patient's total distress, and when the life expectancy is three months or more, surgery for pain may be indicated. Surgery for the mitigation of pain takes two principal forms: 1) interruption of the local pain-conducting pathways, so that the pain stimuli do not reach consciousness; 2) modification of consciousness or personality in its affective state by leucotomy, so that the distressful element of the pain experience is mitigated or abolished.

The indications for pain-pathway interruption are a life expectancy of three months or more and that local physical pain is the major factor in the patient's total distress. One should note that the pain of infected cancerous growths, especially those of the mouth and pelvis, can often be sufficiently controlled by the use of appropriate antibiotics. Local osseous pain of cancerous deposits can often be relieved by appropriate hormonal modifications or by local palliative x-radiation. These measures will be tried in suitable circumstances before resorting to surgery for pain. Examples of pain-pathway interruption are: trigeminal nerve interruption by alcohol injection of its sensory root, followed by cervical sympathectomy to prevent neurotrophic keratitis, for cancer of the face or mouth or jaws. When the disease extends to the throat or neck, surgical division of the glossopharyngeal nerve and upper rootlets of the vagus and posterior roots of upper cervical spinal nerves by a suboccipital operation can be added. For pain due to cancer of the pelvis, and from the lower half of the body, section of the

spinothalamic tract about the second thoracic segment of the spinal cord on one or both sides is the most effective and also the least damaging procedure. It is selective for pain and temperature and does not interfere with other important sensory functions for the limbs; nor does it cause the unpleasant paræsthesiæ associated with more peripheral sensory nerve interruptions. For local pain due to cancer about the thoracic inlet, one can combine spinothalamic tract section at the second cervical level of the cord with division of the upper cervical posterior roots.

These operations of interruption of the local pain-pathway are brilliantly effective and reliable for pain alone, and are ideal in carefully selected cases. They are limited in their sphere of usefulness by their very specificity. They do nothing for other causes of distress of the victim of cancer.

It is in these cases of more multiple causes of distress that leucotomy by modifying the affective receptivity and reactivity removes not only the distressful quality of pain itself but those of the other adverse factors in the cancer case. Patients so treated, when specifically questioned on the subject, will state casually that they can still feel the pain; but they will not complain of it spontaneously and they will not demand or require analgesics. In fact they cease to be distressed by pain and by other adverse developments in the course of cancer. There are, however, limitations upon this treatment also. The patients so treated not only cease to be distressed by pain, but also by moral wrongs, by shameful situations, by the misfortunes of their friends. Nor can they experience with their former depth of feeling the satisfactions and pleasures of life. The alleviation of distress from pain and other troubles is bought at the expense of a flattening or shallowing of the whole affective personality. Such patients will not react with full responsibility or keen judgment to the various problems and situations of life. Our use of this merciful procedure for the cancer victim is limited to the management of cases in which such an irrevocable alteration of personality can be justifiably accepted. I believe that such cases are numerous.

Lastly neurological surgery may be required in cancer to preserve important neurological functions, whose loss would add seriously to the patient's troubles.

Examples are cranial decompression, with or without removal of a local metastatic tumour, to relieve headache and vomiting, to preserve vision, or to preserve other cerebral functions. Similarly it may be necessary to carry out spinal decompression with or without local tumour removal when a cancerous metastasis compresses the spinal cord or nerve roots. This is simply the surgery of brain and spinal cord tumours applied to the cancer patient—with the life expectancy and the specific management of the cancerous neoplasia as the dominant determining factors.

In cancerous compression of the spinal cord, surgical decompression is a procedure of urgency—to be computed in hours, not in days—if the miseries of paraplegia are to be averted. In a majority of these cases the vertebral column is eroded and unstable. Here, rustless steel internal splints, applied to the spinous processes, may enable the patient to become ambulant for his remaining life. In a minority the bones are not involved and such splintage is not required.

Thus, the sufferers from presently incurable cancer, may, in properly selected cases, gain much from neurological surgery—perhaps in securing remission of the disease itself, and certainly in the relief or avoidance of many of its distressing features.

Dr. G. F. Abercrombie:

Most patients do not mind dying, but they do not wish it to be painful. "It must always be remembered that there is in every mortal illness a point beyond which any further attempt at *curative* treatment is not only useless but cruel" (Hutchison, 1926). What is sometimes attempted to-day in the name of palliative treatment ought to be denounced in equally vigorous terms. One of the inescapable duties of the general practitioner, who attends regularly and frequently upon such patients, is to say "Hold! Enough". Let us never forget that excellent aphorism "Morphia exists to be given, and not merely to be withheld".

I think the great majority of these patients would prefer to end their lives in their own homes if it could be done without placing an intolerable burden on their attendants; but unceasing supervision is impossible in these days, and hospitals should make it a point of honour never to refuse to readmit their former cancer patients *in extremis*.

Many surgeons cannot bring themselves, and will not be persuaded, to tell a patient the truth about his malady, and thus they place the general practitioner at a great and lasting disadvantage. That would not matter if the patient were at ease in mind, but all too often he is not. "They tell you nothing in hospital, sir. What is it? What *is* the matter with me?" It is perfectly true that some remain in absolute ignorance, apparently, of the fact that they have an incurable cancer right up to the very end, and they are accounted fortunate; but it really does not follow that they would have fared worse if they had been told the truth. How many practitioners would wish their medical attendants to attempt to deceive them? Do we not all say "If this happens to me, I want to be told. I want to know"?

We ought to give our patients credit for that common sense and courage which we know they possess. Instead, we are afraid to tell them, possibly because we fear they may commit suicide—an extremely unlikely event—or because, mistakenly, we judge them unable to face the suffering, assumed to be inevitable and supposed to be intractable. Cancer has a dreaded reputation, which now needs urgently to be reconsidered. Very many patients' lives end peacefully, and I doubt whether their distress is any greater than that experienced in other terminal conditions.

What happens when patients *are* told that they have cancer and that it cannot be cured? Usually, nothing very noticeable—the information is digested, a mental adjustment is made, and in all probability the subject is never brought up for discussion again. Their kith and kin are spared attempts at dissimulation, the desperate search for remedies ceases, and treatment by analgesics and narcotics is accepted as a matter of course. Certainly, very great care is needed, but I cannot recall that I have ever had good cause to regret telling the truth. The bond of

sympathy and confidence between doctor and patient is thereby drawn closer and holds firmly to the end.

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Professor C. A. Wells: Some of the most difficult problems of palliation may best be considered not by one specialist individual, "the cancerologist", nor by any one general surgeon acting alone, but by a group of individuals, each able to make his own peculiar contribution to the discussion. With the increasing complexity of all therapeutic measures in surgery the time is approaching when many difficult problems such, for example, as that of hypertension must be tackled, not by the general or the specialized physician or surgeon acting alone, but by a group of people associating themselves for the purpose of the study and treatment of particular types of diseases. Only by some such arrangement or by some other method of full and free consultation between different interests will it be possible to offer the best combination of treatment in complicated clinical problems.

Dr. P. W. Nathan: One of our main difficulties in looking after these patients with severe pain is the nursing staff. In this country we are brought up in a puritan culture; and in this culture, it is implied that suffering is a good thing, and that a certain amount of pain is desirable. This view of life seems to afflict nurses with particular severity. It seems to be impossible to persuade them to give enough analgesics.

The question of addiction in these patients with incurable cancer has been raised. What if these patients do die addicts? They are going to die anyway; why should they not die addicted to an analgesic? In any case we find that most of them do not become addicts. All the patients on whom we have done successful pain-relieving operations have not asked for the drugs which they were accustomed to have before the operation.

Dr. Gavey brought up the point about not telling the patient a deliberate lie. I think that this is *the* place for a deliberate lie. For some years we have been doing research on pain-relieving operations on patients with cancer. When I began this work, I imagined that there would be only a few patients to whom one could tell the truth—that they had incurable cancer. Now I believe that there are as good as none. It seems that people cannot stand it. It may be possible sometimes to tell people over 70 or 80; but younger than this, people are not ready to die. This is no problem peculiar to cancer. In neurology we meet many young people who have a fatal illness; it would be cruelty to tell any of them that they are going to die.

Dr. L. Dulake: In view of many comments on the question "should the patient be told of the incurable nature of his disease", I do not feel that any rigid rules can be applied, certainly not that all should be told or that none should be told. In my experience many patients become aware of their condition. A day comes when something in the handclasp, in the expression of the patient, implies acceptance of a hopeless situation. From then on, doctor, patient, and close relations

often find it easier to play a gentle game of "make-believe". Human understanding bridges many gaps.

Mr. Eric L. Farquharson: There is a very good working rule to guide us as to how much a patient should be told, when he is suffering from irremovable cancer. The patient should be told the truth only when it appears certain that he *really* wants to know, or that the information would be of definite benefit to himself or to his family. Even after the most unsuccessful operation, many patients are buoyed up with the hope that cure has been achieved; such hope may remain with them even when it is obvious that they are sinking fast, and it is often their only source of comfort as the darkness closes in. The hospital ward or the specialist's consulting room is seldom the best place to impart such news, and, perhaps more important, the specialist himself is seldom able to judge how much a patient should be told. It seems so much better that, in the exceptional cases where truth must prevail, it should be told by the family doctor, so often an old and trusted friend, in the quietness and privacy of the patient's own home.

Mr. Murray Falconer: Hypophysectomy for parasexual tumours, principally carcinoma of the breast with widespread metastases, is in its infancy, having been introduced by Luft and Olivecrona only two years ago. It is, however, an operation with a low mortality and little morbidity, and regression of the metastases appears to occur in more than half the patients, even after widespread dissemination. The follow-up periods, however, are still short, and so it is not yet possible to compare its merits with those of adrenalectomy. The encouraging results to date, however, indicate that the procedure warrants further trial, and make it difficult to say that there is ever a stage in carcinoma of the breast where treatment should be withheld, because the disease has become advanced and widespread.

Mr. Robert Cox: Many of the previous speakers have spoken about cancer exclusively, but the problems are those of malignant diseases in general, particularly with the wider age distribution of other forms of malignant disease.

The problem as to whether the patient should be told, is clearly different in the aged patient who has already run the full course of his life, as compared with one in middle life. The problem is even more difficult in the young adult, perhaps married and with the responsibility of young children dependent on him, and most of all it seems wrong to inform the patients when they are of tender years.

On the use of morphia those who work in hospital centres which deal with large numbers of late cases of malignant diseases are aware that often the miseries of morphia poisoning are worse than those of the disease for which the drug has been given. Frequently these patients are made much more comfortable by simple nursing care, regularization of their bowels, proper feeding and the withdrawal of morphia either to a reasonable level or its substitution by a simple mixture containing aspirin and opium which, in many cases, is quite adequate to control the pain even of the terminal phases.

Mr. Maurice Ewing: No one in the Discussion has spoken of the experience of the radiotherapist in the palliation of malignant disease. I am sure that a great many of us must often turn to him for help in the control of recurrent cancer in

our surgical failures and I often question whether the irradiation that is given in such cases has, in fact, any real value as a palliative.

Miss G. M. Barry: The question of whether to tell a patient that she is dying of cancer must be settled individually. I have personally been reproached by patients at the eleventh hour for not having told them sooner, as there were various things that they would have wished to do had they had time.

I also think that there are cases in which a large palliative operation carrying a definite mortality rate should not be suggested to a patient who urgently desires to live for a few more months in order to finish a particular piece of work.

MORBIDITY AND MORTALITY IN OLD AGE. A STUDY OF EXPERIENCE IN A MODERN HOME FOR THE AGED. PART V*

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METHODS AND BASIC DATA

(Continued)

Mortality Experience by Specific Cause

The mortality experience of the Home was determined for a number of specific causes of death and was compared with that of the United States.

Sources of data

The name, sex, year admitted, age on admission, date of death, age at death, cause(s) of death, date of withdrawal alive, reason for withdrawal alive, and place of transfer were obtained from the records of the Medical Department of the Home, 1935–1951. All material bearing on the total United States experience was obtained from the yearly issues of Mortality Statistics and Vital Statistics of the United States, 1935–1950.

Method of classification

Since the possible causes of death that can be listed on death certificates run in the thousands, some method of reassembling into a smaller number of more comprehensive groups is needed. The grouping employed by most official agencies is that of the International List of Causes of Death, first adopted in 1893, and revised in 1900, 1910, 1920, 1929, 1938 and 1948.

A large portion of the death certificates filed annually in the United States report two or more diseases or conditions as the cause of death (these multiple diseases are known as joint causes of death). It is obvious that for general statistical purposes, when death is attributed to several causes, one cause must be determined by some accepted method of selection that will make for a degree of uniformity among states and nations.

Prior to 1949, the standard authority used for allocating cause of death when two or more causes were listed was the "Manual of the International List of Causes of Death" (98). The joint-cause relationships in the 1939 Manual are practically the same as those in the edition of 1933. According to the rules of the Manual, a system of priorities is established for recording the cause of

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death when two or more causes are listed. Diabetes mellitus, for example, would be given preference over most conditions, except acute infections, cancer, and violent deaths. As a cause of death, it is preferred over intracranial lesions of vascular origin, chronic nephritis, hypertensive vascular disease, arteriosclerotic heart disease, pneumonia, and coronary heart disease.

Subsequent to 1949, following the recommendation of the World Health Assembly in 1948, a new form of death certificate came into general use in the United States of America and most of the civilized world. "The most important feature of the certification form is its emphasis on the underlying cause, as determined by the attending physician" (99). It can be said that prior to 1949, by use of the Joint Cause Manual, the tendency was to give precedence to communicable diseases, and to emphasize cancer and allied disease and diabetes mellitus; this was done in an attempt to make the mortality statistics reflect morbidity. Since 1949, however, the emphasis has been on the underlying cause of death as determined by the attending physician.

Three different approaches to the classification of cause of death were used in this study.

1. Causes of death were allocated by age group and sex and by specific time-period, for the years 1935–1948, in accordance with the rules of the Manual of the International List of Causes of Death (Fifth Revision) and Joint Causes

TABLE 77

Observed Deaths, Home for Aged and Infirm Hebrews, Allocated by Rules of the Manual of the International List of Causes of Death and Joint Causes of Death (5th Revision), by Age, and by Time-Period

MALES

Cause of Death	1935–1940			1941–1945			1946–1948			Total
	Age			Age			Age			
	60–74	75–84	85–94	60–74	75–84	85–94	60–74	75–84	85–94	
I. All cardiovascular diseases except...	8	8	0	3	6	0	1	6	1	22
A. Coronary disease	17	16	1	6	20	2	3	9	2	87
B. Intracranial lesions of vascular origin	5	7	0	3	8	1	2	3	2	31
C. Chronic nephritis	4	3	3	2	1	1	1	3	2	20
II. Pneumonia and influenza	8	9	4	9	11	8	2	9	3	63
III. Diabetes mellitus	5	3	5	3	3	3	1	4	3	30
IV. Tuberculosis (all forms)	0	0	1	1	1	2	1	3	1	10
V. Accidents (all forms)	0	1	0	1	1	0	0	1	0	4
VI. Carcinoma and other malignant tumours	9	6	1	10	7	3	3	5	4	48
A. Neoplasms of digestive tract and peritoneum	10	8	3	7	8	1	4	9	1	51
VII. Genito-urinary tract infections...	2	3	2	3	1	0	0	1	0	12
VIII. All other diseases	0	0	0	0	0	0	0	0	0	0
Total	68	64	20	48	67	21	18	53	19	378

TABLE 78

Observed Deaths, Home for Aged and Infirm Hebrews, Allocated by Rules of the Manual of the International List of Causes of Death and Joint Causes of Death (5th Revision), by Age, and by Time-Period

FEMALES

Cause of Death	1935–1940			1941–1945			1946–1948			Total
	Age			Age			Age			
	60–74	75–84	85–94	60–74	75–84	85–94	60–74	75–84	85–94	
I. All cardiovascular diseases except...	3	4	1	2	5	0	1	3	0	19
A. Coronary disease	11	14	2	11	13	2	4	12	2	71
B. Intracranial lesions of vascular origin	5	6	1	4	8	1	1	4	1	31
C. Chronic nephritis	2	2	2	1	3	3	2	2	3	20
II. Pneumonia and influenza	10	5	3	3	12	5	3	7	4	53
III. Diabetes mellitus	5	5	1	5	6	2	4	8	3	39
IV. Tuberculosis (all forms)	1	1	0	1	1	0	1	2	0	7
V. Accidents (all forms)	1	0	0	1	0	1	0	0	0	3
VI. Carcinoma and other malignant tumours, except	3	6	2	8	14	3	8	6	5	55
A. Neoplasms of digestive tract and peritoneum	5	8	2	4	9	3	5	7	3	46
VII. Genito-urinary tract infections	2	3	1	1	1	0	2	1	0	11
VIII. All other diseases	0	0	0	0	0	0	0	0	0	0
Total	48	55	15	41	72	20	31	52	21	355

of Death (Tables 77 and 78). These findings were compared with total United States experience for the same time-period, by age and sex, in terms of proportionate mortality.

Proportionate mortality was calculated as follows:

$$\text{Proportionate Mortality} = \frac{\text{Number of deaths from specific disease in stated age group}}{\text{Total number of deaths}} \times 100$$

The significance of differences between cause of death at the Home and the total United States experience was determined by the chi-square test of the goodness of fit with d.f. = 11.[1]

2. Causes of death were allocated by age group and by sex for the years 1949–1950 (Table 85), in accordance with the stipulations of the Sixth Revision of the International List of the Causes of Death. These findings were compared with the total United States experience for 1949–1950, in terms of proportionate mortality. Statistical significance was determined by the chi-square test of the goodness of fit, with d.f. = 9.[2]

3. Finally, deaths in the Home during the period 1935–1951 were apportioned to underlying causes as described in the Sixth Revision of the International Lists (Tables 127 and 128, Chapter V). Whenever possible, the nomenclature

[1] *Cf.* Tables 79–84.

[2] *Cf.* Tables 86 and 87.

TABLE 79

Male Deaths (f), Age Groups 60–94, 1935–1940, Coded According to Rules of 5th Revision, Manual of Joint Causes, Compared with Expected Male Deaths (f') 60–94, Derived from the Vital Statistics of the U.S.A., 1935–1940

Cause of Death	f	f'	$f-f'$	$(f-f')^2/f'$
I. All cardiovascular diseases except	16	46.1	−30.1	19.65
A. Coronary disease	34	13.4	+20.6	31.82
B. Intracranial lesions of vascular origin	12	16.4	−4.4	1.19
C. Chronic nephritis	10	14.0	−4.0	1.14
II. Pneumonia and influenza	21	9.6	+11.4	13.53
III. Diabetes mellitus	13	3.7	+9.3	23.37
IV. Tuberculosis (all forms)	1	3.0	−2.0	1.33
V. Accidents (all forms)	1	7.3	−6.3	5.35
VI. Carcinoma and other malignant tumors, except	16	8.2	+7.8	7.42
A. Neoplasms of the digestive tract and peritoneum	21	10.0	+11.0	12.10
VII. Genito-urinary tract infections	7	4.9	+2.1	0.90
VIII. All other diseases	0	15.5	−15.5	15.5
Total	152.00	152.10	0	$\chi^2 = 133.29$

TABLE 80

Observed Male Deaths (f), Home for Aged and Infirm Hebrews, 1941–1945, Age Groups 60–94, Coded According to Rules of the 5th Revision of the Manual of Joint Causes, Compared with Expected Number of Deaths (f') Derived from Vital Statistics of the U.S.A., 1941–1945

Cause of Death	f	f'	$f-f'$	$(f-f')^2/f'$
I. All cardiovascular diseases except	9	41.0	−32.0	25.16
A. Coronary disease	28	17.2	+10.8	6.78
B. Intracranial lesions of vascular origin	12	14.7	−2.7	0.60
C. Chronic nephritis	4	10.0	−6.0	3.76
II. Pneumonia and influenza	28	5.8	+22.2	84.90
III. Diabetes mellitus	9	2.7	+6.3	14.73
IV. Tuberculosis (all forms)	4	2.2	+1.8	1.47
V. Accidents (all forms)	2	5.6	−3.6	2.48
VI. Carcinoma and other malignant tumors, except	20	9.6	+10.4	11.27
A. Neoplasms of the digestive tract and peritoneum	16	9.3	+6.7	4.82
VII. Genito-urinary tract infections	4	3.4	+0.6	0.11
VIII. All other diseases	0	14.5	−14.5	14.7
Total	136	136	0	$\chi^2 = 170.78$

of the Fifth Revision was retained, so as to maintain continuity of statistics of causes of death. Deaths so allocated were compared for the three time-periods of the study, to see whether any trends existed in mode of death.

The comparisons were made in the following manner. Disease-specific death

TABLE 81

Observed Male Deaths (f), Home for Aged and Infirm Hebrews, 1946–1948, Age Groups 60–94, Coded According to Rules of the 5th Revision of the Manual of Joint Causes, Compared with Expected Number of Deaths (f') Derived from Vital Statistics of the U.S.A., 1946–1948

Cause of Death	f	f'	$f-f'$	$(f-f')^2/f'$
I. All cardiovascular diseases except	8	26.9	−18.8	13.28
A. Coronary disease	14	13.6	+0.4	0.01
B. Intracranial lesions of vascular origin	7	11.2	−4.2	1.57
C. Chronic nephritis	6	5.3	+0.7	0.09
II. Pneumonia and influenza	14	3.1	+10.9	38.31
III. Diabetes mellitus	8	2.0	+6.0	18.00
IV. Tuberculosis (all forms)	5	1.5	+3.5	8.16
V. Accidents (all forms)	1	3.7	−2.7	1.97
VI. Carcinoma and other malignant tumors, except	12	6.3	+5.7	5.16
A. Neoplasms of the digestive tract and peritoneum	14	6.4	+7.6	9.02
VII. Genito-urinary tract infections	1	2.0	−1.0	0.50
VIII. All other diseases	0	8.1	−8.1	8.1
Total	90	90	0	$\chi^2 = 104.17$

TABLE 82

Female Deaths (f), Age Groups 60–94, 1935–1940, Coded According to the Rules of the 5th Revision Manual of Joint Causes, Compared with Expected Female Deaths (f') 60–94, Derived from the Vital Statistics of the U.S.A., 1935–1940

Cause of Death	f	f'	$f-f'$	$(f-f')^2/f'$
I. All cardiovascular diseases except	8	36.9	−28.9	22.63
A. Coronary disease	27	7.0	+20.0	57.14
B. Intracranial lesions of vascular origin	12	15.2	−3.2	0.67
C. Chronic nephritis	6	11.0	−5.0	2.27
II. Pneumonia and influenza	19	7.7	+11.3	16.58
III. Diabetes mellitus	11	4.7	+6.3	8.44
IV. Tuberculosis (all forms)	2	1.3	+0.7	0.38
V. Accidents (all forms)	1	5.3	−4.3	3.48
VI. Carcinoma and other malignant tumors, except	11	7.9	+3.0	1.22
A. Neoplasms of the digestive tract and peritoneum	15	8.0	+7.0	6.13
VII. Genito-urinary tract infections	6	1.1	+4.9	21.82
VIII. All other diseases	0	11.8	−11.8	11.80
Total	118	118	0	$\chi^2 = 152.56$

rates for the various causes of death were determined for the three time-periods by sex. Thus, for males of all ages in the Home (age 60 to 94 years) in the six-year time-interval, 1935–1940, the number of deaths from all cardiovascular disease except coronary disease, intracranial lesions of vascular origin and chronic nephritis was 31 (Table 127, Chapter V). During the same time-interval, the sum of the l_x values for all males was 952 (Table 57, Chapter IV). There-

TABLE 83

Female Deaths (f'), Age Groups 60–94, 1941–1945, Coded According to the Rules of the 5th Revision, Manual of Joint Causes, Compared with Expected Female Deaths (f'), 60–94, Derived from Vital Statistics of the U.S.A., 1941–1945

Cause of Death	f	f'	$f-f'$	$(f-f')^2/f'$
I. All cardiovascular diseases except	7	45.0	−38.0	32.08
A. Coronary disease	26	10.8	+15.2	23.37
B. Intracranial lesions of vascular origin	13	16.7	−3.7	0.82
C. Chronic nephritis	7	10.9	−3.9	1.39
II. Pneumonia and influenza	20	6.3	+13.7	31.67
III. Diabetes mellitus	13	6.7	+6.3	7.12
IV. Tuberculosis (all forms)	2	1.2	+0.8	0.53
V. Accidents (all forms)	2	6.1	−4.1	2.75
VI. Carcinoma and other malignant tumors, except	25	10.4	+14.6	21.98
A. Neoplasms of the digestive tract and peritoneum	16	9.9	+6.1	4.09
VII. Genito-urinary tract infections	2	1.5	+0.5	0.17
VIII. All other diseases	0	7.5	−7.5	7.50
Total	133	133	0	$\chi^2 = 133.48$

TABLE 84

Female Deaths (f'), Age Groups 60–94, 1946–1948, Coded According to the Rules of the 5th Revision Manual of Joint Causes, Compared with Expected Female Deaths (f') 60–94, Derived from the Vital Statistics of the U.S.A., 1946–1948

Cause of Death	f	f'	$f-f'$	$(f-f')^2/f'$
I. All cardiovascular diseases except	4	30.0	−26.0	23.40
A. Coronary disease	18	10.0	+8.0	6.40
B. Intracranial lesions of vascular origin	6	13.9	−7.9	4.48
C. Chronic nephritis	7	6.7	+0.3	0.13
II. Pneumonia and influenza	14	3.7	+10.3	2.86
III. Diabetes mellitus	15	5.0	+10.0	20.00
IV. Tuberculosis (all forms)	3	0.8	+2.2	6.05
V. Accidents (all forms)	0	4.6	−4.6	4.60
VI. Carcinoma and other malignant tumors, except	19	8.4	+10.6	13.38
A. Neoplasms of the digestive tract and peritoneum	15	7.6	+7.4	7.20
VII. Genito-urinary tract infections	3	0.8	+2.2	6.05
VIII. All other diseases	0	12.5	−12.5	12.5
Total	104	104.0	0	$\chi^2 = 107.05$

fore, the disease-specific death rate from cardiovascular disease for males aged 60 to 94, was $\frac{31}{952} \times 1000 = 32.56$. This process was repeated for each cause of death for the three time-periods, and the death rates obtained were compared by the chi-square test of association, d.f. = 2.[3]

[3] *Cf.* Tables 88-91.

TABLE 85

Observed Deaths at the Home for Aged and Infirm Hebrews, Ages 60–94, Coded According to the Sixth Revision (1948) of the International List, for the Years 1949 and 1950

Cause of Death	Males	Females
I. Diseases of the circulatory system, all, (400–468) except	3	3
A. Arteriosclerotic heart disease, including coronary disease (420.0, 420.1, 420.2)	7	8
B. Hypertensive cardiovascular disease (440–443). Hypertensive vascular disease (444–447)	5	8
II. Vascular lesions affecting the central nervous system. (330–334)	6	9
III. Pneumonia (480–483), and influenza (490–493)	7	7
IV. Diabetes mellitus (260)	5	4
V. Malignant neoplasms—all, except, (140–205)	5	8
A. Digestive organs and peritoneum (150–156-A) and (157–159)	4	5
VI. Accidents (all) (E 800-E 962)	0	0
All others	5	3
Total	44	55

TABLE 86

Observed Male Deaths, (f), Home for the Aged and Infirm Hebrews, 1949 and 1950, by Age Groups, (60–94), Coded According to 6th Revision (1948) of International List, by Underlying Causes, Compared with Theoretical Deaths (f') Derived from Vital Statistics of the U.S., 1949 and 1950

Cause of Death	f	f'	$(f-f')$	$(f-f')^2/f'$
I. Diseases of circulatory system, all (400–468) except	3	6.05	−3.05	1.538
A. Arteriosclerotic heart disease including coronary disease (420.0, 420.1, 420.2)	7	12.75	−5.75	2.593
B. Hypertensive cardiovascular disease (440–443). Hypertensive vascular disease (444–447)	5	2.78	+2.22	1.773
II. Vascular lesions affecting the central nervous system. (330–334)	6	4.79	+1.21	0.306
III. Pneumonia (480–483) and influenza (490–493)	7	1.11	+5.89	31.252
IV. Diabetes mellitus (260)	2	0.59	+1.41	3.373
V. Malignant neoplasms—all except (140–205)	5	6.06	−1.06	0.185
A. Digestive organs and peritoneum (150–156A) (157–159)	4	2.88	+1.12	0.435
VI. Accidents (all) (E800-E962)	0	2.39	−2.39	2.39
VII. All others	5	4.61	+0.39	0.05
Total	44	44.01	0	$\chi^2 = 43.85$

Investigation was made of the changes produced in the various categories of cause of death by the different methods of selecting the underlying cause. This was achieved by sampling the causes of death in the population of the Home, for the eleven-year period, 1935–1945. These 288 deaths were assigned to underlying causes by rules of the Fifth and Sixth Revisions (Tables 91 and 92). Ratios were determined in the following manner. Since the deaths for all cardiovascular renal disease were 125 when assigned under the arbitrary rules

TABLE 87

Observed Female Deaths, (f) Home for the Aged and Infirm Hebrews, 1949 and 1950, by Age Groups, (60–94), Coded According to 6th Revision (1948) of International List, by Underlying Causes. Compared with Theoretical Deaths (f′) Derived from Vital Statistics of the U.S., 1949 and 1950

Cause of Death	f	f'	$(f-f')$	$(f-f')^2/f'$
I. Diseases of circulatory system, all (400–468) except	3	8.35	−5.35	3.427
A. Arteriosclerotic heart disease including coronary disease (420.0, 420.1, 420.2)	8	12.52	−4.52	1.632
B. Hypertensive cardiovascular disease. (440–443) hypertensive vascular disease (444–447)	8	5.01	+2.99	1.784
II. Vascular lesions affecting the central nervous system (330–334)	9	7.61	+1.39	1.254
III. Pneumonia (480–483) and influenza (490–493)	7	1.35	+5.65	23.647
IV. Diabetes mellitus (269)	4	1.55	+2.45	3.872
V. Malignant neoplasms—all except (140–205)	8	8.33	−0.33	0.013
A. Digestive organs and peritoneum (150–156A) (157–159)	5	3.61	+1.39	0.535
VI. Accidents (all) (E800–E962)	0	1.87	−1.87	1.87
VII. All others	3	4.80	−1.80	0.675
Total	55	55.00	0	$\chi^2 = 37.619$

of the Fifth Revision, and 180 by the stipulations of the Sixth Revision, $\frac{125}{180} \times 100$ = ratio of Fifth/Sixth Revisions in per cent (Tables 92 and 93). Lastly, an over-all comparison was made of the allocation of all categories of cause of death between the Fifth Revision and the Sixth Revision by means of the chi-square test of the goodness of fit, with d.f. = 10 (Tables 94 and 95).

Interpretation of chi-square values

One of the stipulations of the chi-square test is that all the theoretical frequencies (f′) should be 5 or more. Under circumstances in which some of the values of f′ are less than 5, the test may be used, but it is commonly stated that the results must be interpreted with extreme caution. Thus, the 1 per cent value rather than the 5 per cent value may be assumed to be the border-line of significance. It is noted that in all the chi-square tests (Tables 79–84 and 86–87) there are cells in which the theoretical frequencies are less than 5.

It is of interest that this ultraconservative approach is not necessary. Cochran (100) has shown that there is little disturbance to the 5 per cent level when a single expectation is as low as ½. This is also true for the 1 per cent level, if the number of degrees of freedom in chi-square exceeds 6. Two expectations as low as 1 may be allowed with negligible disturbance to the 5 per cent level. In tests in which all expectations are small, results suggest that the tabular χ^2 is tolerably accurate, provided all expectations are at least 2 (101–103).

In the tests in which there are eleven degrees of freedom (Tables 79–84),

TABLES 88–91

Illustration of Method of Comparing Death Rates by Specific Cause and Time-Period for Residents of the Home for Aged and Infirm Hebrews, 1935–1951

Cause I

Males (all cardiovascular disease, except coronary disease, intracranial lesions of vascular origin and chronic nephritis)*

Rate = 31/952 = 32.56/1000 in 1935–1940
Rate = 31/651 = 47.62/1000 in 1941–1945
Rate = 36/1079 = 33.36/1000 in 1946–1951

TABLE 88. (*f* table)

	Died	Survived	Total	$1000q_x$
	31	921	952†	32.56
	31	620	651†	47.62
	36	1043	1079†	33.36
Total.....	98	2584	2682	36.53 = q_o

* Table 127.
† Table 57.

TABLE 89. (*f'* table)

	Died	Survived	Total
1	34.78	917.22	952
2	23.78	627.22	651
3	39.42	1039.58	1079
Total.....	98	2584	2682

TABLE 90. (*f-f'* table)

	Died	Survived
1.	3.78	−3.78
2.	−7.22	−7.22
3.	−3.42	−3.42

TABLE 91. (f-f'^2/f' table)

	Died	Survived
1.	0.412	0.016
2.	2.192	0.083
3.	0.296	0.011

$\chi^2 = 0.412 - 2.192 - 0.296 - 0.016 - 0.083 - 0.011 = 3.010$, and is not significant statistically.

TABLE 92

Comparison of Observed Deaths in Male Residents of the Home for Aged and Infirm Hebrews, 1935–1945, Coded According to the Rules of the 5th Revision, Manual of Joint Causes, with Observed Deaths, 1935–1945, Allocated by Underlying Causes According to Stipulations of the 6th Revision

Cause of Death	Arbitrary Rules of 5th Revision		Underlying Causes According to Methods of 6th Revision		Ratio, 5th Revision to 6th Revision
	No.	% of total	No.	% of total	
Coronary disease	62	21.5	70	24.3	0.9
Intracranial lesions of vascular origin	24	8.3	41	14.2	0.6
Nephritis	14	4.9	7	2.4	2.0
Other cardiovascular renal diseases	25	8.7	62	21.5	0.4
Total cardiovascular-renal	125	43.4	180	62.5	0.7
Neoplasms of digestive tract	37	12.9	22	7.6	1.7
All other malignant neoplasms	36	12.5	18	6.3	2.0
Total malignant neoplasms	73	25.4	40	13.9	1.8
Pneumonia and influenza	49	17.0	41	14.2	1.2
Diabetes mellitus	22	7.6	13	4.5	1.7
Genito-urinary tract infections	11	3.8	8	2.8	1.4
Tuberculosis	5	1.7	5	1.7	1.0
Accidents	3	1.0	1	0.3	3.0
All other diseases	0	0	0	0	
Total	288	99.9	288	99.9	

TABLE 93

Comparison of Observed Deaths in Female Residents of the Home for Aged and Infirm Hebrews, 1935–1945, Coded According to the Rules of the 5th Revision, Manual of Joint Causes, with Observed Deaths, 1935–1945, Allocated by Underlying Causes According to Stipulations in the 6th Revision

Cause of Death	Arbitrary Rules of the 5th Revision		Underlying Causes According to Rules of 6th Revision		Ratio, 5th Revision to 6th Revision
	No.	% of total	No.	% of total	
Coronary disease	53	21.1	47	18.7	1.1
Intracranial lesions of vascular origin	25	10.0	40	15.9	0.6
Nephritis	13	5.2	6	2.4	2.2
Other cardiovascular diseases	15	6.0	67	26.7	0.2
Total cardiovascular renal	106	42.3	160	63.7	0.7
Neoplasms of digestive tract	31	12.4	17	6.8	1.8
All other malignant neoplasms	36	14.3	25	10.0	1.4
Total malignant neoplasms	67	26.7	42	16.8	1.6
Pneumonia and influenza	39	15.5	28	11.2	1.4
Diabetes mellitus	24	9.6	11	4.4	2.2
Genito-urinary tract infections	8	3.2	3	1.2	2.7
Tuberculosis	4	1.6	6	2.4	0.7
Accidents	3	1.2	1	0.4	3.0
All other diseases	0	0	0	0.0	
Total	251	100.1	251	100.1	

TABLE 94

Comparison of Observed Deaths in Male Residents of the Home for Aged and Infirm Hebrews, 1935–1945, Coded According to the Rules of the 5th Revision, Manual of Joint Causes, with Observed Deaths, 1935–1945, Allocated by Underlying Causes According to Stipulations of the 6th Revision

Cause of Death	f (5th Revision)	f' (6th Revision)	$(f-f')$	$(f-f')^2/f'$
Coronary disease	62	70	−8	0.914
Intracranial lesions of vascular origin	24	41	−17	7.048
Nephritis	14	7	+7	7.000
All other cardiovascular diseases	25	62	−37	22.080
Neoplasms of the digestive tract	37	22	+15	10.227
All other malignant neoplasms	36	18	+18	18.000
Pneumonia and influenza	49	41	+8	1.561
Diabetes mellitus	22	13	+9	6.231
Genito-urinary tract infections	11	8	+3	1.125
Tuberculosis	5	5	0	0.000
Accidents	3	1	+2	4.000
Total	288	288	0	$\chi^2 = 78.186$

The 1% value, $n = 10 = 23.209$.

TABLE 95

Comparison of Observed Deaths in Female Residents of the Home for Aged and Infirm Hebrews, 1935–1945, Coded According to the Rules of the 5th Revision, Manual of Joint Causes, with Observed Deaths, 1935–1945, Allocated by Underlying Causes According to Stipulations of the 6th Revision

Cause of Death	f (5th Revision)	f' (6th Revision)	$f-f'$	$(f-f')^2/f'$
Coronary disease	53	47	+6	0.766
Intracranial lesions of vascular origin	25	40	−15	5.625
Nephritis	13	6	+7	8.167
All other cardiovascular diseases	15	67	−52	40.358
Neoplasms of the digestive tract	31	17	+14	11.529
All other malignant neoplasms	36	25	+11	4.840
Pneumonia and influenza	39	28	+11	4.321
Diabetes mellitus	24	11	+13	15.363
Genito-urinary tract infections	8	3	+5	8.333
Tuberculosis	4	6	−2	0.667
Accidents	3	1	+2	4.000
Total	251	251	0	$\chi^2 = 103.969$

The 1% value, $n = 10 = 23.209$.

the 1 per cent value of P is 24.7. In the tests in which d.f. = 9, as in Tables 86–87, the 1 per cent value of P is 21.7. These 1 per cent values are exceeded greatly in each of the tests and statistical significance is unquestioned. Therefore, since the deviations are obviously significant, whether P = 1 per cent or P = 0.001 per cent is of no practical importance.

Accurate age-specific death rates not obtainable

An alternative method, namely that of comparing age-specific death rates by five-year groups, from 60 to 64 and 90 to 94, could not be used because of the absence of reliable data on age distribution. Breakdown of the population of the United States by year, sex, and five-year age groups from 60 to 94 would be required. These estimates of the total population by five-year age groups for 1935–1951 are not available for intercensal years.

A request for this data to the Bureau of the Census brought the following reply. "We are reluctant to provide greater age detail in our estimates for the aged population because the basic data are not satisfactory. The reporting of age in the census and on death certificates for the aged population has not yet, in our opinion, attained the degree of accuracy required for the preparation of reliable estimates by age. However, figures are shown in this report (1940 and 1950 census years) only for the age groups 75 to 84 and 85 years of age and over. It is open to question whether these census figures or interpolations between them can provide reliable enough base populations for the rates you wish to compute." (104).

Survival of Residents with Certain Chronic Diseases

The three chronic diseases selected for study were coronary heart disease, hypertension, and diabetes mellitus. Included under coronary heart disease were patients with the following diagnoses: coronary thrombosis, coronary insufficiency, coronary arteriosclerosis, and coronary occlusion. Included under hypertension were patients with the diagnoses: hypertension, hypertensive heart disease, and hypertensive cardiovascular disease.

Method of obtaining five-year and ten-year survival rates

Master tables were drawn up for each of the three chronic diseases being studied. The following items were included in the tables: name, sex, year ad-

TABLE 96

Results of the Follow-up of 129 Male Residents of the Home for Aged and Infirm Hebrews with Coronary Heart Disease, between 1935–1951

Year of Follow-up	l_x	w_x	d_x	$l_x - \frac{1}{2}w_x$	$100q_x$	$100p_x$	$100kp_x$	$100kq_x$
0–1	129	1	32	128.50	24.90	75.10	75.10	24.90
1–2	96	0	22	96.00	22.92	77.08	57.89	42.11
2–3	74	1	15	73.50	20.41	79.59	46.08	53.92
3–4	58	0	14	58.00	24.14	75.86	34.96	64.82
4–5	44	1	14	43.5	32.18	67.82	23.71	76.29
5–6	29	0	5	29.00	17.24	82.76	19.62	80.38
6–7	24	0	6	24.00	25.00	75.00	14.72	85.28
7–8	18	0	3	18.00	16.67	83.33	12.27	87.73
8–9	15	0	1	15.00	6.67	93.33	11.45	88.55
9–10	14	0	3	14.00	21.43	78.57	9.00	91.00

Average age on detection of this disease was 73 years.

mitted, age on admission, year of diagnosis, date of death, age at death, year of withdrawal alive, and place of transfer. These master tables then permitted the construction of Tables 96–101, which show the results of the follow-up by Life-Table methods (105) of the residents of the Home with the three selected chronic diseases.

It could not be assumed that the individuals in the groups being studied were of the same chronologic age when the diseases were first detected. However, since the risk of dying within the period specified was so great, and since grouping by chronologic age would have provided groups with such small numbers as to make the study valueless, no grouping or subdivision according to chronologic age was attempted.

Many investigators calculate five-year and ten-year survival rates incorrectly by dividing the number of individuals still alive at the end of the five-

TABLE 97

Results of the Follow-up of 56 Male Diabetics, Residents in the Home for Aged and Infirm Hebrews, 1935–1951

Year of Follow-up	l_x	w_x	d_x	$l_x - \frac{1}{2}w_x$	$100q_x$	$100p_x$	$100hp_x$	$100hq_x$
0–1	56	4	6	54.00	11.11	88.89	88.89	11.11
1–2	46	1	9	45.50	19.78	80.22	71.31	28.69
2–3	36	0	8	36.00	22.22	77.78	55.46	44.54
3–4	28	0	7	28.00	25.00	75.00	41.60	58.40
4–5	21	0	2	21.00	9.52	90.48	37.64	62.36
5–6	19	0	1	19.00	5.26	94.74	35.66	64.34
6–7	18	1	2	17.50	11.42	88.58	31.59	68.41
7–8	15	1	2	14.50	13.79	86.21	27.23	72.77
8–9	12	0	7	12.00	58.33	41.67	11.34	88.66
9–10	5	0	3	5.00	60.00	40.00	4.53	95.47

Average age on detection of diabetes was 74.20 years.

TABLE 98

Results of the Follow-up of 168 Male Hypertensive Residents of the Home for Aged and Infirm Hebrews, 1935–1951

Year of Follow-up	l_x	w_x	d_x	$l_x - \frac{1}{2}w_x$	$100q_x$	$100p_x$	$100hp_x$	$100hq_x$
0–1	168	1	31	167.50	18.51	81.49	81.49	18.51
1–2	136	0	36	136.00	26.47	73.53	59.92	40.08
2–3	100	0	25	100.00	25.00	75.00	44.94	55.06
3–4	75	0	19	75.00	25.33	74.67	36.56	66.44
4–5	56	0	10	56.00	17.86	82.14	27.57	72.43
5–6	46	0	7	46.00	15.22	84.78	23.37	76.63
6–7	39	2	7	38.00	18.42	81.58	19.07	80.93
7–8	30	0	4	30.00	13.33	86.67	16.53	83.47
8–9	26	1	7	25.50	27.45	72.55	11.99	88.01
9–10	18	0	1	18.00	5.56	94.44	11.32	88.68

Average age on detection of this disease was 73.20 years.

TABLE 99

Results of the Follow-up of 114 Female Residents of the Home for Aged and Infirm Hebrews with Coronary Disease, 1935–1951

Year of Follow-up	l_x	w_x	d_x	$l_x - \frac{1}{2}w_x$	$100q_x$	$100p_x$	$100hp_x$	$100hq_x$
0–1	114	2	30	113.00	26.54	73.46	73.46	26.54
1–2	82	0	27	82.00	32.93	67.07	49.27	50.73
2–3	55	0	12	55.00	21.82	78.18	38.52	61.48
3–4	43	0	9	43.00	20.93	79.07	30.46	69.54
4–5	32	0	5	32.00	15.63	84.37	25.70	74.30
5–6	27	0	9	27.00	33.33	66.67	17.13	82.87
6–7	18	0	7	18.00	38.89	61.11	10.47	89.53
7–8	11	0	2	11.00	18.18	81.82	8.57	91.43
8–9	9	0	1	9.00	11.11	88.89	7.62	92.30
9–10	8	0	1	8.00	12.50	87.50	6.67	93.33

Average age on detection of the disease was 73.10 years.

TABLE 100

Results of the Follow-up of 72 Female Diabetic Residents of the Home for Aged and Infirm Hebrews, 1935–1951

Year of Follow-up	l_x	w_x	d_x	$l_x - \frac{1}{2}w_x$	$100q_x$	$100p_x$	$100hp_x$	$100hq_x$
0–1	72	1	12	71.50	16.78	83.22	83.22	16.78
1–2	59	0	19	59.00	32.20	67.80	56.42	43.58
2–3	40	0	10	40.00	25.00	75.00	42.32	57.68
3–4	30	0	5	30.00	16.67	83.33	35.27	64.73
4–5	25	0	2	25.00	8.00	92.00	32.45	67.55
5–6	23	0	0	23.00	00.00	100.00	32.45	67.75
6–7	23	0	0	23.00	39.13	60.87	19.75	80.25
7–8	14	0	3	14.00	21.43	78.57	15.52	84.48
8–9	11	0	6	11.00	54.55	45.45	7.05	92.95
9–10	5	0	0	5.00	00.00	100.00	7.05	92.95

Average age on detection of the disease was 73.40 years.

year or ten-year period by the total population being studied; thus ignoring the mass of information given by the experience of those persons who were in the study for less than the five-year or ten-year period for which rates were computed. It has been proved mathematically (106) that, if the probability of surviving in any year is multiplied by the probability of surviving during the previous years, the most accurate means for finding the probability of surviving in any given length of time has been employed. The procedure followed in constructing Tables 96–101 in which the survival rates were obtained, was as follows: 1) The life-table mortality rate (q_x) was first calculated by the formula $q_x = \frac{d_x}{l_x}$ where l_x was the number present at the beginning of the year and d_x the number who died during the year. 2) A certain number (w_x) of individuals of the groups studied withdrew alive during the year. Each withdrawal

TABLE 101

Results of the Follow-up of 289 Female Hypertensive Residents of the Home for Aged and Infirm Hebrews, 1935–1951

Year of Follow-up	l_x	w_x	d_x	$l_x - \frac{1}{2}w_x$	$100q_x$	$100p_x$	$100{}_hp_x$	$100{}_hq_x$
0–1	289	1	47	288.50	16.29	83.71	83.71	16.29
1–2	241	1	61	240.50	25.36	74.64	62.48	37.52
2–3	179	0	40	179.00	22.35	77.65	48.52	51.48
3–4	139	0	18	139.00	12.95	87.05	42.24	57.76
4–5	121	1	15	120.50	12.44	87.56	36.99	63.01
5–6	105	1	18	104.50	17.22	82.78	30.62	69.38
6–7	86	0	22	86.00	25.58	74.42	22.79	77.21
7–8	64	1	8	63.50	12.60	78.40	19.92	80.08
8–9	55	1	16	54.50	29.35	70.65	14.07	85.93
9–10	38	0	6	38.00	15.79	84.21	11.85	88.15

Average age on detection of this disease was 73.40 years.

alive (w_x) was considered as having had half a year's experience, so that the number at risk for the whole year was taken as $lx - \frac{1}{2}w_x$, and $q_x = \frac{d_x}{l_x - \frac{1}{2}w_x}$.

3) The probability of survival was obtained by subtraction of the probability of death (q_x) from 1, or $p_x - 1 = q_x$. If $100q_x$ was the percentage dying during the year, then $100p_x$ was the percentage surviving through the year. Thus, of the 56 male diabetics entering into the experience (l_x) 4 withdrew alive from the experience during the first year (w_x) and 6 died during the first year (d_x) (Table 97). The number at risk was $56 - \frac{4}{2} = 54$ and the death rate per 100 was $100 \times \frac{6}{54}$, or 11.11 per cent. Therefore, $100 - 11.11 = 88.89$, the percentage surviving the first year. Since 88.89 per cent survived the first year ($100p_x$ column) and 80.22 per cent of those entering the experience in the second year survived the second year, the probability of surviving through two years was $100 \times (.8889 \times .8022) = 71.31$ per cent ($100{}_hp_x$ column). Similarly, the probability of male diabetics surviving five years was $100 \times (.8889 \times .8022 \times 7778 \times .7500 \times .9048) = 37.64$ per cent, and the probability of surviving ten years was $100 \times (.8889 \times .8022 \times .7778 \times .7500 \times .9048 \times .9474 \times .8858 \times .8621 \times .4167 \times .4000) = 4.53$ per cent.

Construction of graphs of survivors

The l_x values needed for the survivorship curves were derived in the following manner. The l_x value at zero year of the follow-up was considered to be 1,000. By applying the survival rates given in the $100{}_hp_x$ columns of Tables 13–18 (Chapter III) the number of survivors in each year of follow-up was obtained. Thus, for male diabetics at zero year of follow-up, $l_x = 1000$. After one year of follow-up, $l_x = 1000 \times .8889 = 889$. After two years of follow-up, $l_x = 1000 \times .7131 = 713$.

Observed survival for each chronic disease was then compared with the survival of the total population of the Home, as derived from the life tables of the Home. Since the average age of patients on detection of the chronic diseases was 73 for five of the six groups being followed, and 74 for the sixth group, comparison was made with the survival values of residents of the Home, age 73. The l_x values for the survivorship curves were derived in the manner previously described in this Chapter. Thus, for males residing in the Home during the period 1935–1951, age 73, the l_x value = 1,000 × 29788/29788 = 1,000. After one year of follow-up, l_x = 174/173 = 26,034/29,788 × 1,000 = 874. This process was repeated for each of ten years of follow-up.

Comparison of chronic-disease survival rates with over-all survival rates for residents of the Home

Comparison was made between the five-year and ten-year survival rates of residents with the selected chronic diseases and the five-year and ten-year survival rates of all residents aged 73 years, as derived from the life tables of the Home. Comparison was made in the following manner. The survival values of residents of the Home, derived from the life tables of the Home, were obtained by dividing the number of survivors at ages 78 and 83 by the number of survivors at age 73, for both sexes. Thus, the probability of a male resident

TABLE 102

Comparison of the Number of Female Residents of the Home for Aged and Infirm Hebrews with Selected Chronic Diseases Surviving for Five Years Compared with the Expected Number of Survivors, Assuming a 51.4 Per Cent Five-Year Survival Rate

	f	f'	$(f-f')^2/f'$
Coronary heart disease	27	58.6	17.05
Diabetes mellitus	23	37.0	5.30
Hypertension	105	148.5	12.74
Total	155	244.10	$\chi^2 = 35.09$

$P < .01$

TABLE 103

Comparison of the Number of Female Residents of the Home for Aged and Infirm Hebrews with Selected Chronic Diseases Surviving for Ten Years Compared with the Expected Number of Survivors, Assuming a 20.2 Per Cent Ten-Year Survival Rate

	f	f'	$(f-f')^2/f'$
Coronary heart disease	7	23.0	11.13
Diabetes mellitus	5	14.35	6.22
Hypertension	32	58.3	11.87
Total	44	95.8	$\chi^2 = 29.22$

$P < .01$

TABLE 104

Comparison of the Number of Male Residents of the Home for Aged and Infirm Hebrews with Selected Chronic Diseases Surviving for Five Years Compared with the Expected Number of Survivors, Assuming a 45.4 Per Cent Five-Year Survival Rate

	f	f'	$(f-f')^2/(f')$
Coronary heart disease	29	58.6	14.95
Diabetes mellitus	19	25.4	1.61
Hypertension	46	76.3	12.03
Total	94	16.03	$\chi^2 = 28.59$

$P < .01$

TABLE 105

Comparison of the Number of Male Residents of the Home for Aged and Infirm Hebrews with Selected Chronic Diseases Surviving for Ten Years Compared with the Expected Number of Survivors, Assuming a 14.81 Per cent Ten-year Survival Rate

	f	f'	$(f-f')^2(f')$
Coronary heart disease	11	19.1	3.43
Diabetes mellitus	2	8.3	4.78
Hypertension	17	24.9	2.51
Total	30	52.3	$\chi^2 = 10.72$

$P < .01$

aged 73 surviving five years = l_{78}/l_{73} = 13,531/29,788 × 100 = 45.4 per cent. Similarly, the ten-year survival rate of a male resident aged 73 = l_{83}/l_{73} = 4,411/29,788 × 100 = 14.81 per cent. Comparison of survival was made by the chi-square test of the goodness of fit, d.f. = 2[4] in the following manner. The numbers of residents with the three selected chronic diseases, surviving for five years were considered as representing the observed frequencies (f). By assuming a 45.5 per cent survival rate, the theoretical frequencies (f') were obtained.

Comparison of Disease-Specific Mortality in the Home With That in Published Reports

Published reports in the medical literature discuss hypertension in patients with unusually severe forms of disease, in patients graded into four categories according to clinical criteria, and in age groups differing from those at the Home. For obvious reasons, the Home does not grade the hypertensive residents. True comparison data for the purposes of comparing the findings at the Home with published papers on hypertension do not exist.

Similarly, few reports of long-term observations on large groups of patients

[4] *Cf.* Tables 102–105.

TABLE 106

Comparison of Five-year Mortality Rates for Hypertensive Residents of the Home for Aged and Infirm Hebrews, 1935–1951, by Sex

	Survived	Died	Total	Rate
Males	47	121	168	72.43
Females	107	182	289	63.01
	154	303	457	66.30

$$\text{S.E.}_{\text{diff.}} = \sqrt{\frac{(66.3)\ (33.7)}{168} + \frac{(66.3)\ (33.7)}{289}} = 4.58$$

$$\text{Dev}/\sigma = \frac{9.42}{4.58} = 2.06$$

TABLE 107

Comparison between the Combined Five-year Mortality Rate (Both Sexes) of Residents of the Home for Aged and Infirm Hebrews, 1935–1951, with Hypertension, and the Five-year Mortality Rate Noted in the Study of Smithwick and Thompson

	Survived	Died	Total	Rate
Combined rate	154	303	457	66.30
Smithwick series	215	252	467	54.00
	369	555	924	60.06

$$\text{S.E.}_{\text{diff.}} = \sqrt{\frac{(60.06)\ (39.94)}{457} + \frac{(60.06)\ (39.94)}{467}} = 3.22$$

$$\text{Dev}/\sigma = \frac{12.30}{3.22} = 3.82$$

TABLE 108

Comparison between the Five-year Survival Rate of Male Residents of the Home for Aged and Infirm Hebrews, 1935–1951, with Angina Pectoris, and the Five-year Survival Rate Noted in the Study of Block and Associates

	Died	Survived	Total	Five-Year Survival Rate
Male (residents of the Home)	97	32	129	23.71
Block's series	2474	3471	5945	58.40

$$\sigma_{p_1} = \sqrt{\frac{58.4 \times 41.6}{129}} = 4.34$$

$$\text{Dev}/\sigma = \frac{34.69}{4.34} = 7.99 \quad P < .01$$

with coronary disease, and still fewer reports with adequate follow-up information were found. Similar conditions prevailed in the literature on diabetes mellitus, and no comparable survival values were noted.

After careful selection, the experience of Smithwick and Thompson (107)

TABLE 109

Comparison between the Five-year Survival Rate of Female Residents of the Home for Aged and Infirm Hebrews, 1935–1951, with Angina Pectoris, and the Five-year Survival Rate Noted in the Study of Block and Associates

	Died	Survived	Total	Five-Year Survival Rate
Female (residents of the Home).....	85	29	114	25.70
Block's series.....	2474	3471	5945	58.40

$$\sigma_{p_1} = \sqrt{\frac{(58.4)\ (41.6)}{114}} = \sqrt{21.31} = 4.62$$

$$\text{Dev}/\sigma = \frac{58.4 - 25.7}{4.62} = 7.08 \quad P < .01$$

TABLE 110

Comparison between the Ten-year Survival Rate of Male Residents of the Home for Aged and Infirm Hebrews, 1935–1951, with Angina Pectoris, and the Ten-year Survival Rate Noted in the Study of Block and Associates

	Died	Survived	Total	Ten-Year Survival Rate
Male (residents of the Home).....	117	12	129	9.0
Block's series.....	3739	2206	5945	37.1

$$\sigma_{p_1} = \sqrt{\frac{(37.1)\ (62.9)}{129}} = 4.26$$

$$\text{Dev}/\sigma = \frac{28.1}{4.26} = 6.6$$

TABLE 111

Comparison between the Ten-year Survival Rate of Female Residents of the Home for Aged and Infirm Hebrews, 1935–1951, with Angina Pectoris, and the Ten-year Survival Rate Noted in the Study of Block and Associates

	Died	Survived	Total	Ten-Year Survival Rate
Female (residents of the Home).....	106.40	7.60	114	6.67
Block's series.....	3739	2206	5945	37.10

$$\sigma_{p_1} = \sqrt{\frac{(37.1)\ (62.9)}{114}} = \sqrt{20.47} = 4.52$$

$$\text{Dev}/\sigma = \frac{37.1 - 6.67}{4.52} = 6.73 \quad P < .01$$

was chosen for purposes of comparison in hypertension, as it appeared to have fewer noncomparable features with the Home than the other studies. Comparison was made between the five-year mortality rate of Smithwick and Thompson and the combined five-year mortality rate for the male and female

TABLE 112

Results of Follow-up of 47 Male Residents of the Home for the Aged and Infirm Hebrews who Were Sent Out to Mental Institutions, 1935–1951

Years after Being Sent Out	Number Living Last Observed between x and $x+1$	Number Dying between x and $x+1$	Number Present at Beginning of the Year	Effective Number Present at Beginning of the Year	Probability of Dying during the Year	Probability of Surviving during the Year	Cumulative Probability of Surviving during Specified and Preceding Years
x	w_x	d_x	l_x	$l_x - \frac{1}{2}w_x$	q_x (per 100)	p_x (per 100)	$100hp_x$
0–1	3	23	47	45.5	50.55	49.45	49.45
1–2	0	10	21	21.0	47.62	52.38	25.91
2–3	0	3	11	11.0	27.27	72.73	18.84
3–4	1	2	8	7.5	26.67	73.33	13.82
4–5	0	1	5	5.0	20.00	80.00	11.06
5–6	0	1	4	4.0	25.00	75.00	8.30
6–7	0	0	3	3.0	00.00	100.00	8.30
7–8	0	1	3	3.0	33.33	66.67	5.53
8–9	0	0	2	2.0	00.00	100.00	5.53
9–10	0	0	2	2.0	00.00	100.00	5.53

TABLE 113

Results of Follow-up of 51 Female Residents of the Home for Aged and Infirm Hebrews Who Were Sent Out to Mental Institutions, 1935–1951

Years after Being Sent Out	Number Living Last Observed between x and $x+1$	Number Dying between x and $x+1$	Number Present at Beginning of the Year	Effective Number Present at Beginning of the Year	Probability of Dying during the Year	Probability of Surviving during the Year	Cumulative Probability of Surviving during Specified and Preceding Years
x	w_x	d_x	l_x	$l_x - \frac{1}{2}w_x$	q_x (per 100)	p_x (per 100)	$100hp_x$
0–1	2	17	51	50.00	33.33	66.67	66.67
1–2	2	10	32	31.0	31.25	68.75	45.84
2–3	1	3	20	19.5	15.38	84.62	38.79
3–4	1	5	16	15.5	32.26	67.74	26.28
4–5	0	2	10	10.0	20.00	80.00	21.02
5–6	2	1	8	7.0	14.29	85.71	18.02
6–7	0	1	5	5.0	20.00	80.00	14.42
7–8	1	0	4	3.5	00.00	100.00	14.42
8–9	0	1	3	3.0	33.33	66.67	9.61
9–10	1	0	2	1.5	00.00	100.00	9.61

hypertensive patients of the Home, by applying the normal curve in the computation of the standard error of the difference and the relative deviate[5].

The report of Block and associates (108) was selected for comparison with the experience with coronary disease in the Home. Comparison was made between the five-year and ten-year survival rates of Block and associates and similar survival values for the male and female residents of the Home with

[5] *Cf.* Tables 106 and 107.

TABLE 114

Results of Follow-up of 98 Former Residents of the Home for the Aged and Infirm Hebrews Who Were Sent to Mental Institutions 1935, 1951

Years after Being Sent Out	Number Living Last Observed between x and $x+1$	Number Dying between x and $x+1$	Number Present at Beginning of the Year	Effective Number Present at Beginning of the Year	Probability of Dying during the Year	Probability of Surviving during the rear	Cumulative Probability of Surviving during the Specified and Preceding Years
x	w_x	d_x	l_x	$l_x - \frac{1}{2}w_x$	q_x (per 100)	p_x (per 100)	$100kp_x$
0–1	5	40	98	95.5	40.82	59.18	59.18
1–2	2	20	53	52.0	38.46	61.54	36.42
2–3	1	6	31	30.5	19.67	80.33	29.25
3–4	2	7	24	23.0	30.43	69.57	20.35
4–5	0	3	15	15.0	20.00	80.00	16.28
5–6	2	2	12	11.0	18.18	81.82	13.32
6–7	0	1	8	8.0	12.50	87.50	11.66
7–8	1	1	7	6.5	15.38	84.62	9.87
8–9	0	1	5	5.0	20.00	80.00	7.90
9–10	1	0	4	3.5	00.00	100.00	7.90

TABLE 115

Conversion of the Death Rates of Camargo and Preston to Life Table Death Rates*

Years after Being Sent Out	Number Living Last Observed between x and $x+1$	Number Dying between x and $x+1$	Number Present at Beginning of he Year	Effective Number Present at Beginning of the Year	Probability of Dying during the Year	Probability of Surviving during the Year	Cumulative Probability of Surviving during the Specified and Preceding Years
x	w_x	d_x	l_x	$l_x - \frac{1}{2}w_x$	q_x (per 100)	p_x (per 100)	$100kp_x$
0–1	21	111	239	238.50	46.54	53.46	53.46
1–2	1	23	107	106.50	21.60	78.40	41.91
2–3	0	18	83	83.00	21.69	78.31	32.82
3–4	2	11	65	64.00	17.19	82.81	27.18
4–5	1	14	52	51.50	27.18	72.82	19.79
5–6	0	9	37	37.00	24.32	75.68	14.98

* Camargo, O., and Preston, G. H.: Reference 109, Table 5, p. 171.

coronary disease, by applying the normal curve to determine the standard error of the difference and then calculating the relative deviate[6].

Comparison of Psychiatric Mortality with That in Published Reports

Letters were sent to state mental hospitals housing former residents of the Home, requesting information about date of admission, date and cause of death, if dead, and date of discharge and institution to which transfer was made, if discharged. From the replies it was possible, by life-table methods,

[6] *Cf.* Tables 108–111.

TABLE 116

Comparison of the Probability of Survival in State Mental Institutions of Former Residents of the Home for Aged and Infirm Hebrews Who Were Transferred to Mental Institutions, 1935–1951, and Patients in the State Mental Hospitals of Maryland

EXAMPLE: The probability of surviving the first year

	Died	Survived	Total	Per Cent Survived
Former residents of the home	40	58	98	59.18
Maryland State Mental Hospital patients	111	128	239	53.46
Total	151	186	337	55.19

$$\text{S.E.}_{\text{diff.}} = \sqrt{\frac{55.19 \times 44.81}{98} + \frac{55.19 \times 44.81}{239}} = 5.98$$

$$\text{Dev}/\sigma = 5.72/5.98 = 0.96$$

to construct Tables 112–114, which show the results of the follow-up of the 98 former residents of the Home who were sent to mental hospitals.

Comparison was made between the mortality experience of residents of the Home transferred to mental institutions and that of patients, 65 years of age and over, residing in the state mental hospitals of Maryland as reported by Camargo and Preston (109) on the basis of a six-year follow-up. In order to make the comparison, it was necessary to convert the death rates reported by Camargo and Preston to life-table death rates.

The discharged patients in the series of Camargo and Preston were considered as withdrawals alive. Each person so withdrawn was counted as having been exposed to (and survived) a half year's experience, so that the number at risk for the whole year was taken as $l_x - \frac{1}{2}w_x$, and $q_x = d_x/l_x - \frac{1}{2}w_x$. A table was then drawn up (Table 114) which shows the results of the follow-up over a six-year period for residents of state mental hospitals in Maryland aged 65 years and over.

Comparison was then made between the survival rates for each of the six years of follow-up calculated from the data of Camargo and Preston (Table 115) and the corresponding rates for the former residents of the Home (Tables 112–114), by applying the normal curve to determine the standard error of the difference, and then calculating the relative deviate.[7]

(To be continued.)

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[7] *Cf.* Table 116.

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RAUWOLFIA TRANQUILIZATION FOR THE DISTURBED AGED

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Man's eternal search for renewal of youth has led inevitably to increased longevity at old age and, instead of the carefree life envisioned, to the problems of senescence. The promising hopes and advances of modern medical science have ironically produced a maladjustment of American human ecology, in that the greatly increased life expectancy has not been accompanied by adequate provision for the integration of our older citizens into our social and economic structure.

The impact of increased longevity has caught us unprepared and has produced radical economic and social changes, but the greatest impact has been in the world of medicine. Medical care of the aged can no longer be considered incidental; geriatric medicine is of foremost importance in meeting the challenge of an aging population. In the United States today, there are 11.5 million people in the age-group 65 years and older, representing 7.5 per cent of the total population. Their number has quadrupled during the last half century. In 1900, there were 3 million; by 1975, there may be close to 20 million (1).

The Jewish Community of Los Angeles is attempting to meet its responsibilities in this area by providing facilities at the Jewish Home for the Aged. This institution now has an average population census of 300. The minimum eligible age for admission is 65, the average being 72. The average age of the residents is 79; the youngest is 65 and the oldest, 100.

The policy of the Home is to accept only those who are physically and mentally self-sufficient, not excluding those with serious chronic illnesses, providing they are ambulatory at the time of admission. This admission policy is liberally interpreted in favor of accepting borderline applicants, and many of the residents show the stress of senescence and senile maladjustment. Since it is also the policy of the Home to keep their residents unless they become a hazard to themselves or to others, an active psychiatric program has been instituted in an effort to reduce emotional disturbances and improve tranquility as an aid to management. This treatment includes psychotherapy, chemotherapy and electrotherapy.

The present report deals with our latest psychiatric regimen, in which two of the currently acclaimed Rauwolfia drugs were used as tranquilizing agents. Reserpine[1], a single alkaloid of *Rauwolfia serpentina* and the alseroxylon fraction[2], a mixture of selected Rauwolfia alkaloids, were chosen for clinical trial. Both drugs had been used for hypertension by the Medical Staff at the Home for some time, and their relative safety and clinical efficacy confirmed.

In addition to their anti-hypertensive action, an outstanding effect of the

* Address: 6360 Wilshire Boulevard, Los Angeles 48, California.

[1] Serpiloid, supplied through the courtesy of Riker Laboratories, Inc., Los Angeles, California.

[2] Rauwiloid, also supplied through the courtesy of Riker Laboratories, Inc.

Rauwolfia drugs is that of a non-hypnotic sedative (2). It is a virtue of these agents, moreover, that their concomitant hypotensive and sedative effects do not limit their use to hypertensive patients. Broad clinical experience has shown that they can be used in normotensive patients without any significant hypotensive effect. Their mild sedative or tranquilizing action has, therefore, been utilized for amelioration of symptoms in the emotionally disturbed (3–5).

PROCEDURE

Nineteen residents of the Home were selected for treatment with Rauwolfia drugs. They were chosen by the attending psychiatrists, I. W. Ruskin, M.D. and James Weishaus, M.D., because of exhibiting one or a combination of such symptoms as agitation, depression, confusion, delusions, hallucinations, and generally disturbed behavior. Eighteen of these patients were treated only for emotional disturbances; the nineteenth was also treated for intractable pain due to cancer. They were continued under observation by members of the social service, nursing, psychiatric and medical staffs. The procedure was as follows:

After an initial interview by a psychiatrist, treatment was started with reserpine (Serpiloid), 2 mg. daily, in two doses. The patients were observed daily by the nursing personnel and interviewed at weekly or bi-weekly intervals by one or both authors. At these times their blood pressures were checked and observations were made as to behavior, attitudes, tranquility, state of activity, appetite, habits of sleep, communication and well-being. The dosages were readjusted as necessary, and continuing observations were made.

There was a wide range of individual response to the two Rauwolfia drugs. Although it was possible to determine an average dose requirement, the optimal dosage for each individual varied greatly and could be established only by repeated observation. It was found that reserpine (Serpiloid), 2 mg. daily divided into two doses, was a good basis from which to start. After one to two weeks on this dosage schedule, a calming, relaxing effect could usually be noted in those patients in whom the drug was effective. Dosage was then decreased by half. If, however, the patient continued to be agitated or hallucinatory, dosage was increased to 3 mg., and even 4 mg. daily, and observation was continued for two or three weeks. If a salutary effect on the emotional state was obtained, the dosage was reduced gradually by 1-mg. amounts over a period of several weeks until a maintenance level of 0.5 to 1 mg. daily was reached.

After two months of reserpine therapy, patients were changed to alseroxylon (Rauwiloid) therapy, starting with a dosage of 8 mg. daily. Again this was individually increased or decreased, depending on the patient's reaction to the drug over a period of several weeks. Although dosages of alseroxylon ranged between 4 mg. and 12 mg. daily, the 8-mg. dosage on the average was satisfactory for maintenance. From the rather limited experience of this study, it appeared that there was not a great deal of difference in the effectiveness of the two drugs: patients showing satisfactory improvement on reserpine, maintained this improvement when changed to alseroxylon. If no improvement was induced with reserpine therapy, alseroxylon also had little effect.

TABLE 1

Results of Rauwolfia therapy in 19 disturbed aged patients

	Patient	Age	Sex	Symptoms	Dosage of Serpiloid	Months of Therapy	Results
1.	AF	74	F	Paranoid delusions, aggressive attitudes. Senile psychosis.	0.25 mg. t.i.d. to 1 mg. b.i.d.	10	Some temporary improvement, but regressed to previous state despite therapy.
2.	BB	80	F	Paranoid delusions.	1 mg. t.i.d., inc. to 4 mg. daily, dec. to 0.5 mg. daily.	6	Distinct improvement; decrease in tension, more easily managed.
3.	BM	87	F	Senile psychosis. Paranoid delusions, hallucinations.	0.25 mg. t.i.d. to 3 mg. daily. Changed to 4 mg. Rauwiloid.	14	Distinct improvement; delusions less disturbing; decrease in anxiety. Continuing therapy.
4.	MB	87	M	Senile psychosis. Depression, confusion and agitation; feeling of rejection.	0.25 mg. t.i.d. to 1 mg. t.i.d.	3	Improvement; less confused and agitated.
5.	SR	69	M	Paranoid delusions, agitation and depression, bizarre somatic symptoms, weight loss, fatigue.	0.25 mg. t.i.d. to 5 mg. t.i.d.	13	Distinct improvement; relief of symptoms; over-all sense of well-being. Continuing therapy.
6.	SD	77	F	Hostile and aggressive behavior; deterioration in self-hygiene.	0.25 mg. t.i.d. to 1 mg. b.i.d., dec. to 1 mg. at bedtime	8	Improvement; more manageable, less incontinent.
7.	WF	71	F	Disturbed, anxious, complaining, demanding.	0.25 mg. t.i.d. to 0.25 mg. q.i.d. Changed to 4 mg. Rauwiloid t.i.d. Stabilized at 1 mg. Serpiloid b.i.d.	7	Slight temporary lessening of symptoms, but no real improvement.
8.	WR	85	F	Chronic brain syndrome; senile psychosis. Confused, disturbed, quarrelsome, aggressively demanding; paranoid delusions.	0.25 mg. t.i.d., dec. to 0.25 mg. b.i.d., to 1 mg. at bedtime	4½	Improvement; less agitated.
9.	BM	75	F	Involutional psychotic reaction.	2 mg., inc. to 3 mg. daily. Changed to 8 mg. Rauwiloid.	11½	General improvement in activity, communication and appearance.

10.	LR	71	F	Emotional instability with somatization. Restless, demanding.	0.25 mg. t.i.d.	5	Improvement; quieter and less demanding.
11.	NG	75	F	Senile psychosis with paranoid and agitated depression, alternating with aggressive dependency.	5 mg., dec. to 2 mg. daily.	6	Improvement; less agitated.
12.	KH	73	M	Paranoid delusions and aggressive behavior, especially prior to prostatectomy.	0.75 mg., to 3 mg. daily. Changed to 8 mg. Rauwiloid.	8	Improvement; quieter and less of a management problem.
13.	HS	76	F	Cerebral arteriosclerosis with psychosis and agitation. Hyperactive, incontinent. A serious management problem.	0.25 mg., inc. to 2 mg. daily. Changed to 8 mg. Rauwiloid. Testestrin, Thorazine and Metrazol added.	5½	Same temporary improvement in contact and control but regressed despite further therapy.
14.	WB	86	M	Confusion, lack of comprehension, complete disorientation, extreme memory lapses. Occasionally violent.	0.25 mg. t.i.d.	5	Improvement; quieter and more easily managed.
15.	YD	86	M	Mild senile psychosis plus systemic senescence. Cancer of tongue with metastasis; pain.	1 mg. to 2 mg. daily	5	Distinct improvement; easier communication, better appetite, decreased pain.
16.	CH	69	F	Psychoneurosis. Anxiety reaction with restlessness and preoccupation with somatic complaints. Colitis.	0.5 mg. to 1 mg. daily.	4½	Improvement; quieter, less restless; decreased anxiety.
17.	SA	74	F	Anxiety reaction with agitation and depression.	0.75 mg. to 2 mg. daily.	4	No improvement.
18.	LK	79	F	Confusion and disorientation.	0.5 mg. t.i.d. to 1 mg. t.i.d. Changed to Rauwiloid, 4 mg. mg. b.i.d.	3½	No improvement.
19.	WP	86	F	Psychoneurosis. Anxiety reaction with aggression. Demanding; somatic complaints.	1.5 mg. daily.	7	Improvement; less demanding; some decrease in anxiety.

Some residents of the Home received as much as 6 mg. of reserpine daily for several weeks, and 1 patient received a total of 24 mg. of alseroxylon daily for five days, with no untoward results.

RESULTS

The data are listed in Table 1. Of the 19 patients treated primarily for their emotional disturbances, 4 showed definite improvement on Rauwolfia, in that they lost their hallucinations and their marked agitation. They returned to their former status of well behaved individuals. Ten showed improvement which was less marked, but was sufficiently satisfactory to indicate the value of maintaining therapy. In this group was the patient with intractable pain due to cancer. Not only did he experience considerable relief from anxiety, but also appeared to have amelioration of the pain. In general, the patients became quieter, more easily managed, and required less attention from the medical personnel than before treatment with Rauwolfia.

The 5 remaining patients were classified as unimproved by Rauwolfia therapy. Although 3 of these appeared to show slight temporary improvement early in the study, continuation of therapy was accompanied by regression of their condition, despite increased dosage. Because of severe manifestations, 1 patient was also given combined testosterone-estrogen therapy, chlorpromazine, and Metrazol, without satisfactory improvement.

Although the series of cases reported here is small, and the clinical situation did not allow definite controls, it is felt that the results demonstrate the value of Rauwolfia therapy in the emotionally disturbed elderly patient.

Side-effects

Side-effects of therapy with these two Rauwolfia drugs were mild and usually could be overcome by dosage adjustment. Five of the patients complained of being weak and drowsy when taking 2 mg. of reserpine daily. This complaint disappeared when the dosage was reduced to 1 mg. daily. Three patients noticed nasal stuffiness, 2 after using alseroxylon, and 1 after using reserpine. The latter patient also complained of nightmares for several weeks while receiving 2 mg. of the drug daily. The nightmares ceased two days after the dosage was decreased to 1 mg. Four patients were noted to have bradycardia, with pulse rates of 46, 50, 54, and 60, respectively. None, however, had any complaints referable to the reduction of the heart beat, but did mention a concomitant feeling of weakness. The patient with the pulse rate of 46 also had diarrhea during treatment with 0.75 mg. of reserpine daily. This disappeared when the dosage was reduced to 0.5 mg. daily.

Another patient in this series, an alert woman of 67, had a history of colitis. She asked to be included in this study because she was tense, anxious and excitable. Although symptoms of colitis (loose and frequent stools) at first caused her to discontinue medication, subsequent therapy with larger doses indicated that the diarrhea in this patient was due to increased emotional tension, rather than to a physiologic effect of the drug. She was able to continue taking 1 mg. of reser-

pine daily; her bowel movements became normal, and there was a satisfactory tranquilizing effect.

In addition to the foregoing side-effects, many of these patients reported a noticeable increase in appetite. This observation was confirmed by the ward personnel. Since it is extremely difficult to get the elderly patient to eat a complete, well-balanced meal, this increased appetite is a most desirable effect of Rauwolfia therapy.

CONCLUSIONS

1. The Rauwolfia drugs, reserpine and the alseroxylon fraction, are very effective for sedation of the disturbed, aged patient.

2. In the dosages used in this study of 19 patients, there was little difference in the effects of the two drugs.

3. The Rauwolfia drugs deserve a place in the armamentarium of geriatric medicine.

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TOPICAL STEROID THERAPY IN THE OLDER AGE GROUP

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Among a group of 1,200 patients treated with topical steroid preparations for a variety of inflammatory skin conditions, 60 were "elderly," *i.e.*, between 60 and 90 years of age. It long has been felt that senile skins do not absorb medication as well as do younger skins. Therefore, special attention was paid to this group in order to note whether the clinical response to topical therapy paralleled the degree of absorption of the material applied. This report covers the results of our observations.

The average age of the patients in this study was 66 years; there were slightly more females than males. No attempt was made to treat these 60 patients differently from the 1,140 who comprised the rest of the observed group. Using steroid preparations of varying strengths, paired simultaneous comparisons were made in as many instances as possible. The same technique was used to evaluate the effectiveness of the steroid preparations against the vehicle alone and occasionally against some of the more commonly used ointments such as petrolatum, ammoniated mercury, and boric acid. Precautions were taken to keep the patient from knowing the identity of the material with which he was being treated.

The hydrocortisone preparations[1] under investigation contained a fixed amount of neomycin but the content of the hydrocortisone varied from 0.5 per cent to 2.5 per cent. The hydrocortisone was supplied as the acetate salt in several different vehicles in the form of ointments, creams and lotions. A small number of the patients received treatment with the hydrocortisone in the same strength, but as the free alcohol instead of the acetate.

Among the 60 cases studied, there were 14 of lichen simplex chronicus, 8 of anogenital pruritus, 12 of severe and prolonged contact dermatitis, 6 of seborrheic dermatitis, and 4 of stasis dermatitis. The remaining cases were infectious eczematoid dermatitis, dishidrosis and nummular eczema.

The cutaneous lesions in this group of elderly patients responded unusually well to the hydrocortisone-containing preparations. In this respect, our findings agreed with those obtained in the rest of the 1,200-patient survey. In fact, the lesions in the older patients responded better to the steroid topical medications than did those in the younger patients. The percentage of improvement and cure was higher in the older than in the younger age group. The 2.5 per cent material was the most effective; the 0.5 per cent strength seemed the least satisfactory. The 1 per cent material was somewhat less effective than the stronger preparation, but seemed adequate for most of the conditions treated. So far as the vehicles were concerned, there was no marked superiority of one over the others.

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[1] Supplied by the Upjohn Company, Kalamazoo, Michigan.

NUTRITIONAL DEFICIENCY DUE TO AGE AND PHYSIOLOGIC STRESS; ITS CONTROL BY FOOD AND HORMONES*

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The problem of health is of primary concern with older people. Our studies (1) have emphasized that body nutrition is a major factor in the control of their health. The initial change from the normal physiology which leads to different disease entities may be of a similar character, but the primary variations that occur depend upon what tissues are affected to the greatest degree. Thus kidney disease, coronary heart disease, cerebral sclerosis or mental disease may be dependent upon the same basic body nutritional change, and result in arteriosclerosis—general or focal. The location of the more advanced changes in an organ may be the factor which gives rise to a particular disease. As we know it today, the problem of geriatric medicine is not only to recognize and treat diseases that are associated with age but to understand the mechanism or mechanisms involved in the occurrence of disease and thereby control health past mid-life. Such an approach provokes the necessity of considering the mechanisms concerned in the development of a disease phenomenon and especially the loss of properly balanced nutritional status of the older person. We and others (2) have shown that the reaction of the body as it ages increasingly resembles that of an organism under stress as far as body nutrition is concerned. It is known that stress is accompanied to a greater or less degree by a disturbance of the nitrogen balance with a loss of protein from the body and changes in the lipoprotein pattern. There is often an increased diabetic tendency. Our findings and those of others have indicated that such phenomena may be observed at different ages, but are particularly important in the older person. In the elderly, the management of disturbed nutrition, such as the replacement of protein and the maintenance of nitrogen balance, is a greater problem than in other age groups (3–5) and in states of debilitation. Factors such as infection, emotional states, surgery, accidents, endocrine disturbance, or poor nutrition (6) can cause a considerable loss of protein and a negative nitrogen balance in older people for relatively long periods of time. It may be difficult for them to recover from this state, even though there is a return to nitrogen equilibrium. Since it has been established that the administration of hormones may help control nitrogen loss, at least partial relief, from a nutritional standpoint (3) might be expected to result from a better understanding of their action. An understanding of the body needs must be emphasized. As an example, we might point to the relationships involved in the administration of a hormone, such as thyroid. In a state of hypothyroidism, adequate doses of thyroid gland substance enable the organism to retain protein. On the other hand, in euthyroid, or , especially, in hyperthyroid individuals,

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or during administration of exceedingly large doses of thyroid substance, the opposite may occur, and the result is an unfavorable nutritional effect associated with nitrogen loss and body deterioration.

It has been recognized that under conditions of stress there are modifications of function of the endocrine glands (2). An increase in the activity of the mobilization factors of the body, which is the result of stimulation of the pituitary and adrenal glands, thus occurs (7). Age itself results in a change in the functioning level of the endocrine system and more especially a shift to relatively increased activity of the pituitary and adrenal glands compared to the other endocrine glands (8). One may say, therefore, that age is a modified body-stress action, from the standpoint of the change in the endocrine system. The relative increase in adrenocortical activity results in a continuous state of mobilization of food substances, minerals and the like, and thus a waste of body tissue substance. Since the stress-like phenomenon is an important concern in the nutrition of older people and hence in their health, it is well that we understand the response of the body to nutritional changes and especially to loss of protein.

We have shown that the different endocrine substances play a role in protein metabolism, both in the retention and loss of the substance (8). In our earlier studies, we reported on the effect of different hormones given alone, and noted the influence on nitrogen balance in elderly subjects. We showed that androgens have the greatest protein-sparing effect and that cortisone or corticotropin (ACTH) causes a considerable increase in nitrogen excretion and often a marked negative nitrogen balance, as well as an increased tendency to diabetes in the elderly (8). The action of the other exogenous hormones, as far as the nitrogen balance was concerned, depended on whether or not they supplied a body need.

From the standpoint of protein loss, the administration of corticotropin or of cortisone to the average older individual may be considered the equivalent of physiologic stress in causing increased nitrogen loss. Androgens, estrogens, and to a lesser extent other endocrine substances, have a protein-sparing effect when needed by an organism and thus, under such circumstances, may be considered physiologic antagonists to stress factors in regard to protein metabolism. In order to study this aspect of the problem, an investigation of the effect of both single and simultaneous administrations of several hormones on the nitrogen balance was undertaken. In particular, we were interested in observing whether a higher protein intake and the administration of other hormone substances would have a neutralizing action on the catabolic action of stress such as occurs with the administration of cortisone and corticotropin.

MATERIAL AND METHODS

The subjects used in these studies were all inmates of the St. Louis Chronic Hospital. Many of them had been used in our previous studies (5, 8, 9). All were free from acute or infectious diseases at the beginning of the test periods. All received a physical examination and a laboratory work-up which included basal metabolic rate, blood nonprotein nitrogen level, glucose tolerance, complete blood count and urinalysis. Those with evidence of heart disease, diabetes or

nephritis were excluded from the study. The ages of the subjects ranged from 65 to 92 years; the majority were between 70 and 80 years old.

During the studies the subjects received a well-balanced diet yielding about 35 calories per kilogram of body weight per day, and a constant protein intake of either 0.7 or 1.0 gram of protein per kilogram of body weight per day during the different periods of observation. The diets were very similar to those used in our previous studies of nitrogen balance. The technique of performing the nitrogen balance study with regard to such items as regulation of intake, or collection and analysis of samples was the same as that previously reported (5).

Study 1. The endocrine gland substances were given singly, the protein intake was 1.0 gram per kilogram of body weight.

Study 2. New gland substances were added without stopping the previous hormone administration and the subjects had a protein intake of 0.7 gram per kilogram of body weight.

Study 3. The protein intake was 1.0 gram per kilogram of body weight and thyroid, testosterone and protein-zinc insulin (PZI) were started together. Later cortisone, corticotropin and estradiol (Progynon) were added.

In all three studies, after the subjects had been thoroughly accustomed to the diet and to the balance routine, a control period of seven weeks was established during which the nitrogen balance alone was determined.

RESULTS

Thyroid study

After the controlled observation, thyroid was administered in a daily dosage of 16 to 65 mg. to various individuals. During the first twenty days there was

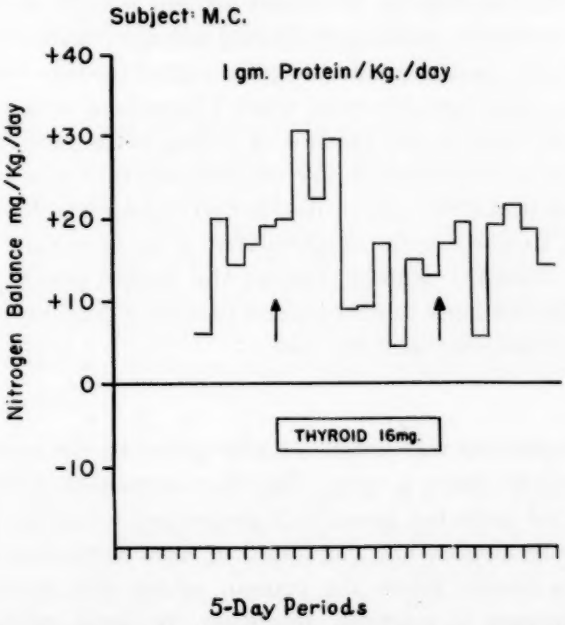

FIG. 1. Effect of thyroid on nitrogen balance in a 78-year-old white man. Note the increase in nitrogen retention during the first twenty days, followed by a decrease.

TABLE 1

The Effect of Thyroid Administration on Nitrogen Balance

Subject	Dosage of Thyroid (mg./day)	Average Nitrogen Balance (mg./Kg./day)					
		Before Admin. (35 days)	During Administration of Thyroid			After Discontinuation	
			First 20 days	Next 30 days	Total, 50 days	25 days	40 days
MC	16	18.2	25.7	11.2	17.0	16.9	16.5
DE	32	10.9	26.6	19.2	22.2	21.4	18.7
TA	48	19.5	26.4	25.9 (5 days)		Cerebral emboli	
KO	65	13.8	18	16.7	17.1	16.7	16.4
OS	16	34.6	39.3	*43.8*	*42.1*	*34.2*	*32.6*
AD	32	11.5	20.3	*41.6*	*33.2*	*30.6*	*27.2*
MA	48	29.5	31.3	*38.3*	*35.2*	*35.2*	
KI	65	*32.9*	*36.0*	*23.5*	*28.5*	*24.1*	*23.9*

The subjects received a diet containing 1.0 Gm. of protein per Kg. of body weight, except during the periods denoted by the italicized figures; in these periods 1.5 Gm. of protein was administered.

increased protein retention. It is of clinical importance that the greatest rise was obtained with 32 mg. of thyroid daily, which would suggest that such a dosage was the optimal one for older individuals such as our patients. After the early period of retention there was a loss of nitrogen during continuation of thyroid therapy for an additional thirty days (Fig. 1). In 3 patients, the protein intake was temporarily raised from 1.0 gram to a level of 1.5 grams in order to note the influence of an increased protein intake on the depression of protein retention caused by prolonged thyroid administration. It was found that any increased nitrogen retention due to the increased protein intake occurred for only a brief period; there was retention when 1.0 gram of protein was given, and then there was a decrease in the amount of nitrogen the body retained.

The observations on the effect of thyroid administration in elderly euthyroid individuals indicate that there is an initial period during which nitrogen retention is increased. This, to our minds, suggests that even in normal elderly patients there is a relative need for protein. During the second period, after the initial need is satisfied, the hormone tends to cause excessive combustion and increased metabolism with consequent nitrogen loss.

Androgen study

Testosterone propionate was independently given to the patients in doses of 25 mg. intramuscularly twice a week. The diet contained different amounts of protein which varied from 0.5 gram to 2 grams per kilogram of body weight. A variation in nitrogen retention was found in most instances, depending upon the level of protein intake. When the protein intake was increased, there was a proportional increase in nitrogen retention. In some subjects the dietary protein intake was constant, and in some it was decreased temporarily. Definite

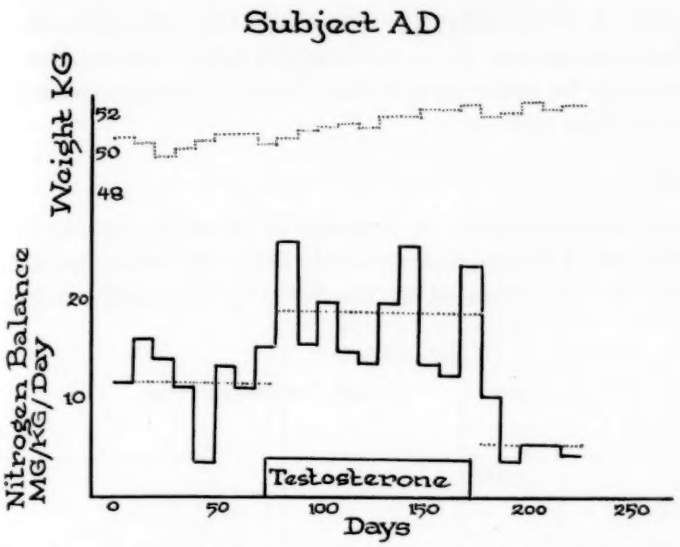

FIG. 2. Effect of testosterone (25 mg. intramuscularly twice weekly) on nitrogen balance in an 80-year-old white man. The diet contained 0.7 Gm. of protein per Kg. of body weight.

nitrogen retention was noted when the testosterone was administered (Fig. 2). This occurred not only when the protein intake was increased, but when it remained constant or was decreased. In patients in whom the protein intake was varied in association with the administration of testosterone, there was an alteration in nitrogen retention in the same direction as the modification of the intake. Our observations suggest that androgen therapy in elderly patients protects against factors which cause nitrogen loss, but does not entirely prevent nitrogen loss under conditions of a low-protein intake.

Estrogen study

Estrogen was given to the patients independently of all other hormones, under dietary conditions in which the protein was either constant, or at different levels. It was found that estrogen (Progynon–B, 1 mg. subcutaneously daily) had no influence on nitrogen retention in the subjects who had an intake of 0.7 gram or better, even when the intake was changed in either direction. However, in the subjects who had a low protein intake of 0.5 gram per kilogram of body weight, there was an increase in the retention of nitrogen. In those whose protein intake was reduced from a higher level to a lower one, estrogen had little or no influence on nitrogen retention.

Insulin study

Protamine zinc insulin was used in small doses of 5 to 10 units in order to study its influence on protein metabolism. It caused some nitrogen retention (Fig. 3), particularly in subjects who had a glucose tolerance curve in which blood sugar values were high, even though the curve was not diabetic in type. There was no evidence that it had any influence in subjects who had other forms of abnormal sugar tolerance curves. This finding suggests that the better combustion of

carbohydrate which occurs after the administration of insulin results in protein sparing. It has been shown by us and others that carbohydrate, particularly sugar, administered to older people may have a protein-sparing action for a certain period of time (10).

Cortisone study

The effect of cortisone alone on a group of patients was studied during two different periods (8). The first was relatively brief; the second lasted for six weeks. The brief study was necessitated by the fact that adequate medication was not

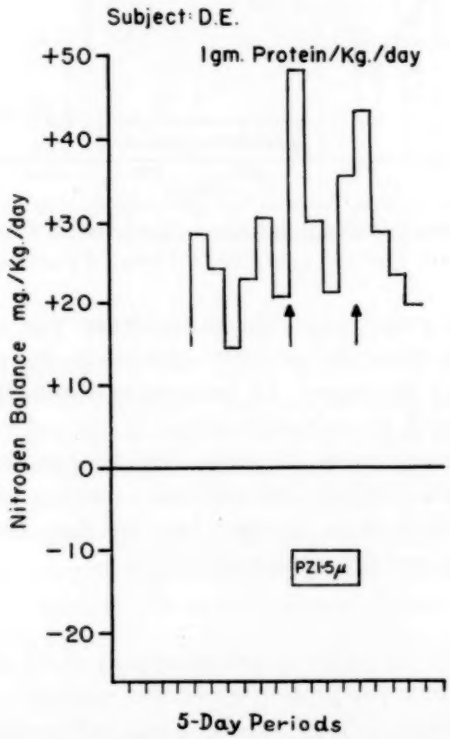

FIG. 3. Effect of protamine-zinc insulin on nitrogen balance in a 93-year-old white man. Note the increased nitrogen retention during the first period of PZI administration. The patient's glucose tolerance curve was of the delayed-return type.

available at the time. Throughout the two periods, each patient received 100 mg. of cortisone per day. It was noted that, beginning with the second five-day period of study, there was a definite drop in nitrogen retention, which reached the maximum decrease on the fifteenth to the twentieth day (Fig. 4). All subjects showed a negative balance. The degree varied from −13 to −31 mg. of nitrogen per kilogram of body weight. Cortisone on both occasions produced certain clinical changes. The patients showed a sense of well-being which started the first or second day after the administration of the hormone and continued throughout the entire period. Some complained of blurring of vision in the second week. Two had a sense of weakness, and 1 had increased thirst and polyuria. Edema of the

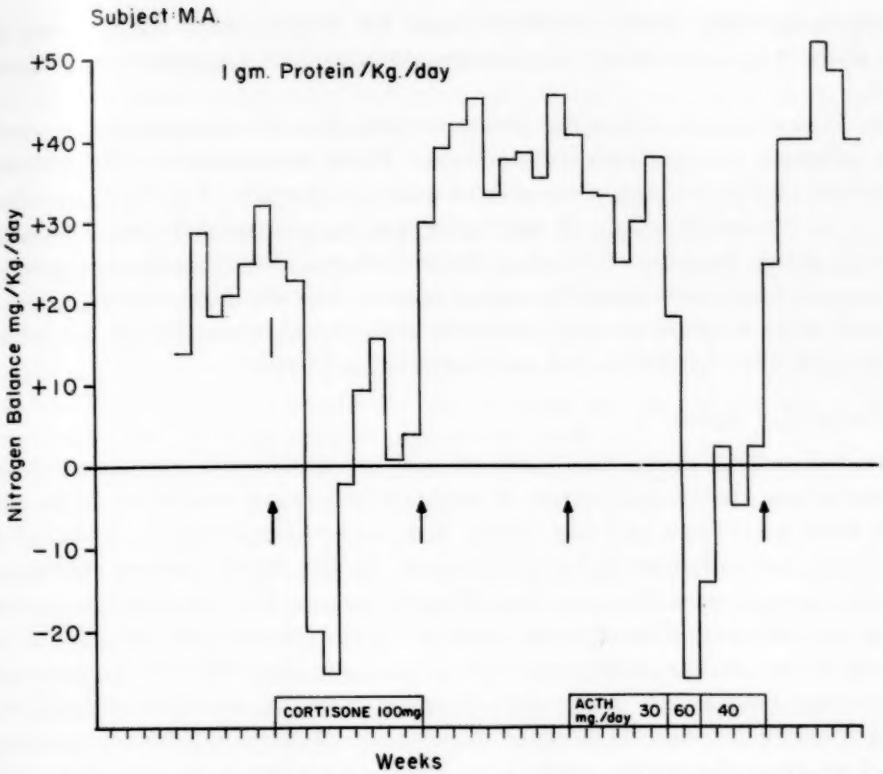

FIG. 4. The effect of single administrations of cortisone and corticotropin (ACTH) on nitrogen retention in a 78-year-old white man. The diet contained 1 Gm. of protein per Kg. of body weight.

extremities and moon-face occurred in varying degrees. After cessation of cortisone therapy, there was general depression accompanied by inability to concentrate, irritability and easy fatigability. It should be emphasized that in this entire period the protein intake remained constant at 1 gram per kilogram of body weight and that there was negative nitrogen balance throughout. After a period of approximately thirty days (the duration of the study being forty-five days), in most of the subjects there was a tendency for nitrogen retention to return to the preadministration level and even to exceed it in some instances.

We have no explanation as to why the subjects reacted differently, except that the 2 who showed during the whole study an increased response to the various administered hormones showed a greater response or increased action when cortisone was administered.

Corticotropin

After an interval of fifty days, when the effect of cortisone had worn off, corticotropin (ACTH) was given in doses of 15 mg., 30 mg. and 45 mg.; for the next thirty days 3 of the subjects received 60 mg., and later 40 mg. daily. Corticotropin caused changes which were similar to those noted when cortisone was given, but to a lesser degree in all instances. Nitrogen retention always dropped,

the maximum drop being correlated with the largest dose. After twenty-five days there was a tendency for nitrogen retention to increase toward normal levels.

The clinical results following the administration of corticotropin resembled those following administration of cortisone. There was a gain in weight, swelling of the feet and limbs, and a notable increase in appetite. The desirable effects, such as an increased feeling of well-being and an increased desire to be active, were not noted, however. Following the withdrawal of corticotropin, the subject tended to be less active mentally and physically, but the degree of depression did not tend to be as great as after cortisone withdrawal, even though the subjects experienced some weakness and continued to be "tired."

Coordination of studies

Our studies have shown that corticotropin or cortisone alone produces changes in metabolism (particularly that of protein) which are similar to those which result from conditions of body stress, such as acute infections, emotional disturbances, cardiac failure and acute diseases. In the elderly, these conditions are generally associated with a negative nitrogen balance (7). The findings may lead to a better understanding of stress itself, since the adrenal and the pituitary are believed to be predominantly active in stress, and the different hormone substances may play a part under such circumstances. It, therefore, seemed to us that a study of the simultaneous administration of these substances was important. A program was set up in which the gland substances were given in a manner which was thought to represent the situation during the initial hormone depletion of the body. Thus thyroid, estrogen, androgen, and insulin were given in that order, in dosages which were the same as those previously given when the substances were administered alone. The exceptions were thyroid, of which the dosages were 16 and 32 mg. daily; and protamine zinc insulin, of which the dosage was increased to 15 units daily in 3 subjects.

Successive addition of hormone substances

The subjects were prepared and observed in a manner similar to that of the initial study. Three of them had been used by us in a previous study, and 4 were new. Thyroid was administered in dosages of 16 and 32 mg. daily for a period of three weeks (Table 2). An anabolic effect, similar to that in the first study, was observed during the first twenty days. Estradiol-benzoate (Progynon-B) was then given to the patients in dosages of 1 mg. daily subcutaneously. Throughout the period there was an increased rate of nitrogen loss. The question of whether the decreased retention of nitrogen was due to the estrogen or to the continuance of thyroid could not be answered. It is our feeling that the lowering of nitrogen retention was the result of thyroid activity, which the estrogen was not able to counteract. There may have been a synergistic action between the thyroid and estrogen, which caused a disturbance of metabolism. The finding of Meites (11) that there was a reduction in growth when these two substances were administered simultaneously in young animals suggests such a conclusion. The thyroid

and estrogen were administered for forty-two days; then testosterone propionate was given in a dosage of 25 mg. intramuscularly twice a week. There was an immediate increase in nitrogen retention, which later tended to drop in some instances. Testosterone was evidently capable of stimulating resistance to the depleting action of the thyroid. It is interesting that the greatest degree of nitrogen retention after testosterone administration occurred in the 2 oldest patients. Perhaps they needed androgen more than did the younger ones.

Insulin was given for a period of thirty-five days, and initially there was a tendency toward an increased nitrogen retention. When the blood sugar levels were elevated, adjustment of insulin administration to the period of increased nitrogen retention and the sugar tolerance curve, resulted in an increase in the conservation of protein. Apparently the increase in the combustion of carbohydrate protects the body against protein loss (10).

Next, cortisone was given in dosages of 25 mg., 50 mg. and 100 mg. daily to different subjects over a period of forty-nine days (Table 2). Cortisone induced the same type of reaction as when given alone, but there was a lesser degree of protein loss. A greater response was noted in the 2 oldest patients, who received relatively small doses of the cortisone compared to some of the younger subjects. This would thus suggest that older persons are more likely to exhibit hyperresponsiveness to the administration of cortisone. It indicates also that older persons are more reactive to the hormones that cause nitrogen depletion, even though they are being treated with gland substances which tend to conserve body protein.

Corticotropin (ACTH) was given in dosages of 15 mg., 30 mg. and 45 mg. daily. It caused a decrease in nitrogen retention in the 2 oldest individuals. In the other subjects, only slight changes or none at all were noted. This is in marked

TABLE 2

Average Nitrogen Retention (mg. per Kg. Body Weight) during the Administration of Different Hormones. The Diet Contained 0.7 Gm. of Protein per Kg. Body Weight

Subject	Without Medication	Thyroid	Thyroid, Progynon	Thyroid, Progynon, Testosterone	Thyroid, Progynon, Testosterone, PZI	Thyroid, Progynon, Testosterone, PZI, Cortisone	Thyroid, Progynon, Testosterone, PZI, Cortisone, ACTH
DE	13	22 (32)*	16	28	15.6 (15)	6.2 (25)	6 (15)
MA	18	24 (16)	15	15	22 (15)	8.5 (50)	11.6 (30)
KO	10	19 (32)	6	15	19.8 (15)	8.1 (100)	8 (45)
BOS	18	19 (32)	12	14	8 (10)	7.1 (25)	10 (15)
RE	18	22 (16)	15.5	15	13 (10)	6 (50)	Expired
HA	17.5	19 (32)	17	18	Cerebral hemorrhage		
BO	16	14 (16)	14.5	11	11 (10)	15 (100)	16 (45)
No. of days	84	21	42	70	35	49	35

* The numbers in parentheses indicate the dosage of the added substance (the last mentioned) in milligrams or units. The dosage of estradiol benzoate (Progynon-B) was 1 mg. subcutaneously daily; and of testosterone propionate, 25 mg. intramuscularly twice a week, in all subjects.

contrast to the effect of corticotropin when administered alone to these people. Thus, when corticotropin was given along with other hormones, the degree of nitrogen loss was much less than that noted when corticotropin was given alone (12). Not only was the nitrogen loss less, but the duration of the loss was shorter.

Simultaneous administration of hormones

A third study was carried out in order to determine the influence of estrogen on nitrogen balance, the influence of a higher protein intake (1 Gm. per Kg. of body weight) on nitrogen retention, and the influence of the simultaneous administration of hormones on the stress factor. We began with the administration of thyroid, insulin and testosterone, and later added cortisone and corticotropin (Table 3). After the patients had received a diet containing 1 Gm. of protein per Kg. of body weight (without hormones) for a period of three months, testosterone, thyroid and insulin were started simultaneously, and continued for a period of one hundred and five days in order to give the body time to adjust to these hormones.

Cortisone was then administered in a dosage of 25–100 mg. daily. The reaction was similar but less marked than when cortisone was given alone (Table 3). It generally resembled that observed in the second study. None of the patients showed a negative nitrogen balance, although they all showed an initial drop. When corticotropin (ACTH) was added to cortisone, there was 1 instance of negative nitrogen balance. However, the total effect of nitrogen loss was not greater than in the other subjects, since in this case the nitrogen balance was lower throughout the entire study.

TABLE 3

Average Nitrogen Retention (mg. per Kg. Body Weight) during the Administration of Different Hormones. The Diet Contained 1.0 Gm. of Protein per Kg. Body Weight

Subject	Without Medication	Thyroid*, Testosterone*, PZI*	Thyroid, Testosterone, PZI, Cortisone**	Thyroid, Testosterone, PZI, Cortisone, ACTH**	Thyroid, Testosterone, PZI, Progynon*	Thyroid, Testosterone, PZI, Progynon, Cortisone, ACTH
DE	28.5	47.6	54.3	34.7	60.3	63.6
MA	31.6	33.0	27.6	27.2	34.0	23.3
EI	6.5	14.6	13	15.5	15.6	27.3
HE	55.5	55.0	47.3	43.7	48.6	54
ST	20.5	21.1	23.3	11	40	29.6
VB	17.5	19.8	3.0	8.25	20.6	27.3
WE	28.6	33.6	36.3	34.7	49.3	19.6
BOR	46.6	41.5	47.6	44.2	40	47
No. of days	42	98	21	28	21	21

* The dosage of thyroid was 16 mg. orally daily; of testosterone propionate, 25 mg. intramuscularly twice weekly; of protamine zinc insulin, 5 units daily; and of estradiol benzoate (Progynon-B), 2 mg. subcutaneously daily, for all 8 subjects.

** The dosage of cortisone acetate was 25 mg. and of corticotropin (ACTH) 15 units intramuscularly daily in the first 4 subjects; but in the last 4 subjects the dosages were 100 mg. and 40 units, respectively.

In order to study the influence of estrogen on these subjects, cortisone and corticotropin were stopped, and Progynon-B, 2 mg. daily, was added. There was an immediate rise in nitrogen retention which was believed to be the result of discontinuance of cortisone and corticotropin. When these two hormones were given again, there was a slight decline in nitrogen retention but the degree of decline was never such as it had been when they were given before to the same subjects, without estrogen. The findings suggest that estrogen has a protective action against body stress as manifested by nitrogen loss.

DISCUSSION

In evaluating the data on the influence of hormonal substances on nitrogen balance, it is seen that thyroid, in dosages of 16 to 65 mg. daily, caused a definite rise in nitrogen retention. The best results were noted with the dosage of 32 mg. daily. This seemingly beneficial effect of thyroid upon nitrogen retention was observed only during the first twenty days of its administration; after that there was a decrease in retention.

This can be explained by assuming that the organism needed a small amount of thyroid, and that the anabolic effect of the thyroid lasted only while there was a deficiency of thyroid hormone in proportion to the other gland substances. When the relative need was supplied, further administration resulted in an abnormally increased amount of the substance in the body; a stress reaction resulted, and a catabolic state developed. There is a relative deficiency of all hormones in older individuals. Thus when a hormone is given, even when there is good evidence that there is a marked deficiency, a disturbance of metabolism may ensue. This disturbance may resemble overactivity of the gland concerned, if the frequency and amount of the dose are not properly controlled. The result is a decrease in nitrogen retention. Since it may be demonstrated that the patient's over-all need for the hormone is not satisfied, we are forced to assume that the reaction is due to a disturbance of the balance between hormones. Thus the administration of thyroid may create a relative deficiency of the other gland substances and thereby cause the stress reaction.

In the study of nitrogen balance, we wished to determine the influence of protein administration on the depleting action of thyroid. In 3 subjects, the protein intake was raised to 1.5 Gm. per Kg. of body weight. The degree of nitrogen retention increased, but in due course the tendency to nitrogen loss returned. Such a finding suggests that an increased protein intake protects the body from a certain form of nitrogen depletion, such as that which occurs during prolonged administration of thyroid, at least during the first two to four weeks. After the elapse of that time the increased protein intake no longer had the power of assisting the body to retain nitrogen in an increased amount.

In the second study, *i.e.*, the addition of one hormone after another, thyroid was followed by estrogen. This combination gave us an opportunity to evaluate estrogen with regard to its ability to help the body retain protein. Since estrogen was administered during the catabolic period of the thyroid effect, the extended period of thyroid influence on the nitrogen balance resulted in a further decrease in nitrogen retention. The estrogen, in the doses given, was too weak to curb such

a stress-like reaction. However, in the third study, estrogen did seem to protect the body from the increased nitrogen loss following administration of cortisone and corticotropin. The increased nitrogen retention apparently caused by estrogen may have been due to the cessation of corticotropin and cortisone. Against this latter consideration is the finding that the decrease in nitrogen retention which occurred when cortisone and corticotropin were again started, was less than it had been previously without estrogen.

The action of exogenous estrogen raises points which need much more attention than the study of nitrogen balance. In our third study, the administration of estrogen seemed to improve the clinical state. It has been demonstrated that thyroid and estrogen each have a peculiar selective function of inhibiting growth in immature animals of both sexes when given separately; but when given together, the degree of growth inhibition is greatly increased because of premature ossification of the bones (11). Thyroid has been shown to increase the action of estrogen when administered in moderate amounts to sterilized female monkeys. It has thus been established that a synergistic action exists between these two hormones (12).

One of our earlier studies showed that moderate estrogen medication in elderly female subjects showing a positive nitrogen balance produced no marked changes in nitrogen retention. There was an increase in calcium retention in those subjects who initially showed a negative calcium balance.

Testosterone, in our experience, had a rather marked effect on the retention of nitrogen, varying to a certain degree with the level of protein intake level and the health of the subjects. The older the individual, the greater the influence of testosterone on the nitrogen balance, indicating that the need for androgen was greater in older patients than in younger ones. In our second study, when testosterone was added to the thyroid and estrogen, it counteracted the catabolic effect of thyroid (which estrogen was unable to do) and improved nitrogen retention. Androgen given alone had an anabolic effect on the body, and was the outstanding substance among those studied in controlling nitrogen loss and increasing nitrogen retention. It is our belief that the action of testosterone was enhanced by the addition of other hormones, with the exception of the mobilizing ones—cortisone and corticotropin. The greatest effect on body nutrition is obtained by coordinate action of the hormones, rather than from a single gland substance. The question then arises whether the degree of lowered nitrogen retention seen in older people is due to a lower androgen content of the body or to a lower content of one or more of the other hormones. Testosterone increases the retention of both calcium and nitrogen when given in moderate to large doses (13–16).

Results of insulin administration indicate that this substance plays a role in protein conservation. In those patients whose glucose tolerance curve was elevated or normal and whose carbohydrate utilization was seemingly poor, its effect was greatest. This observation suggests that its effect was on the combustion of carbohydrate, which acts by sparing protein (17), and not by direct action on the combustion of protein. There appeared to be a parallel between the influ-

ence of insulin on carbohydrate metabolism and utilization and its influence on the retention of nitrogen. A better understanding of body needs and sounder evaluation of the biologic state of the older person are important and necessary for the control of the wasting process that occurs with age.

Sirek and Best (18) demonstrated a relationship between pancreatic function and the nonprotein nitrogen level of the blood. In normal dogs, intramuscular injection of testosterone propionate was followed by a fall in the concentration of NPN. In depancreatized dogs without insulin administration, testosterone did not cause a lowering of the NPN level, such as occurred after insulin was given. Correlation of these findings with ours leads us to assume that our elderly patients fell into a class of insulin-deficient subjects, much as did the depancreatized animals. Such an assumption would establish a deficiency of insulin in all of our subjects, but since the glucose curves were not of the diabetic type, a relative hormone balance must have existed (18). The protein anabolic function of the male sex hormone is intimately associated with the presence of insulin in the body.

This study shows that a balanced hormonal state favors less depletion of nitrogen when the patient is subjected to stress factors, such as the administration of cortisone and corticotropin, or aging. It should be emphasized that proper evaluation and study of the individual is necessary before administering hormones. If too much of any hormone substance is given, there may be a disturbance of metabolism reflected by a protein loss. Nitrogen depletion of the organism may occur when there is a relative excess of circulating hormone substances.

Clinical considerations

In a clinical study of geriatric medicine the functioning of the body should be evaluated in different ways: 1) the degree of ability to utilize food, and 2) the degree of hormonal capacity, particularly the percentage relationship of the compounds that induce assimilation (thyroid, androgen, estrogen, insulin) versus those that induce mobilization (corticotropin, cortisone). Particularly in persons in whom the substances that stimulate nitrogen mobilization are predominant, *e.g.*, in older people, the stress mechanism is brought into play more readily (as when cortisone is administered). Our studies reveal that diet, and especially the proper protein fraction, is an important factor in nutrition under conditions of stress, although protein intake cannot alone prevent the loss of nitrogen. The oldest subject of our group (DE) demonstrated a greater nitrogen depletion when cortisone was given alone with a diet containing 1 Gm. of protein per Kg. of body weight. A comparatively smaller negative nitrogen balance was noted under the stress of cortisone, even during a period of lower protein intake (0.7 Gm. per Kg. of body weight) and administration of assimilative hormones such as testosterone, thyroid, estrogen and protamine zinc insulin (Fig. 5). In the third study, DE, on a diet of 1 Gm. of protein per Kg. of body weight, showed much less decrease in nitrogen retention when protected by previous and simultaneous hormone administration (Fig. 6).

Subjects MA and KO showed a negative nitrogen balance up to −31 mg. for six periods when cortisone was given alone. They showed only a moderate de-

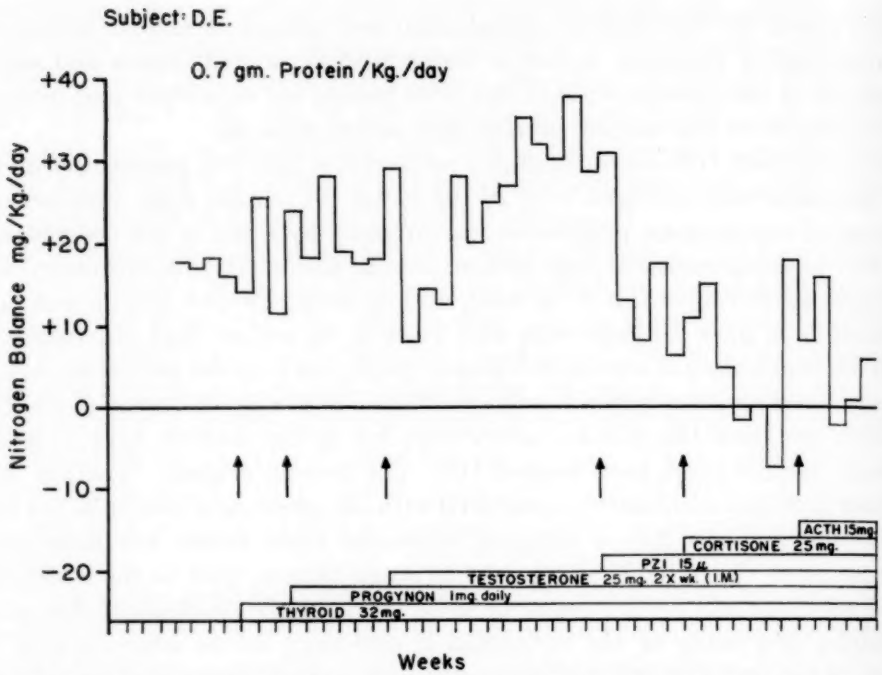

FIG. 5. Effect of various added hormone substances on nitrogen retention in a 93-year-old white man. The diet contained 0.7 Gm. of protein per Kg. of body weight. Note that thyroid and estrogen (Progynon) induced some retention. When testosterone was added, nitrogen retention was significantly increased. During treatment with cortisone and corticotropin (ACTH), there was nitrogen loss.

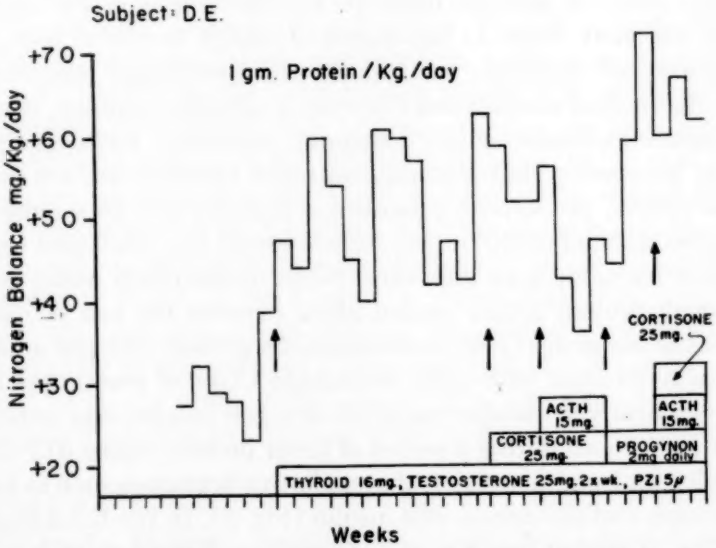

FIG. 6. Same subject as in Figure 5, with the dietary protein increased to 1.0 Gm. per Kg. of body weight. Note the significant increase in nitrogen retention caused by the simultaneous administration of thyroid, testosterone and PZI. The loss induced by cortisone and ACTH was much less than that noted in Figure 5.

crease in nitrogen retention on a low-protein diet (which should have favored depletion when receiving cortisone) due to protection by other hormones (19).

Our results suggest that hormonal deficiencies play an important role in the loss of nutrition in the older organism, introducing a state of nutritional stress. The nutritional reaction to such a hormonal deficiency appears to depend upon the immediate state of body nutrition and the type of hormone involved.

In older persons, hypofunction of any or all of the glands of internal secretion may occur. When the hypofunction is corrected, there is an increased retention of protein and a lessening of the nutritional stress. However, if correction is made for only one hormone, there may be a decreased retention of protein. A fine line has to be drawn between what is needed and what is not. Administration of any hormone, without adequate clinical study, may upset nutrition in an older person. On the other hand, when exact needs are determined, administration results in protection.

In the elderly, nutrition is geared to the mobilizing gland substances (corticotropin and cortisone), which eventually lead to nitrogen depletion. Food substances can be mobilized to a point beyond the ability of the body to utilize them; as a consequence, wasting occurs. Without proper endocrine balance, a more or less constant state of stress exists.

It would seem that estrogen acts differently under different circumstances. Given in combination with thyroid, it induces nitrogen depletion. However, when given in combination with a group of hormones, or when given alone with a low-protein diet, it prevents nitrogen loss.

Careful clinical evaluation before and during the administration of endocrine substances to older people is essential. When endocrine balance is restored by the administration of needed hormonal substances, nutrition and certain aspects of health are assured. On the other hand, when endocrine balance is further disturbed by the improper administration, even of needed hormonal substances, nutrition and health suffer. Stress is thereby introduced and body degeneration is accentuated.

SUMMARY

There are two principal nutritional functions of the hormones in aging persons. One has to do with utilization and restoration of protein in the body, and is well exemplified by the actions of androgen, insulin, thyroid and estrogen. The other has to do with mobilization of food substances and tissues in the body, and is exemplified by the actions of cortisone and corticotropin which, when predominant, result in loss of body tissue. Our studies suggest that in older people disturbed nutrition caused by various stress factors may be relieved by the proper use of hormones. Proper use involves careful clinical evaluation of the need for administration, emphasizing 1) an understanding of any or all deficiencies that may be present, and 2) the appreciation of medical values as far as stress factors are concerned. Elderly or debilitated persons who are, or are likely to be subjected to stress should be protected by correction of endocrine deficiencies.

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CONSTIPATION IN ELDERLY PATIENTS DUE TO DRUG THERAPY

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Constipation in elderly patients presents a variety of problems and must be looked upon from the broadest point of view by the physician. This frequent complaint of the elderly concerns physicians in practically every special field of medicine, as well as the general practitioner.

Although it has been stated that 1 in every 4 older persons is habitually constipated because of dietary inadequacy, drug therapy also plays an important etiologic role. Most elderly patients are receiving some type of drug therapy for a variety of diseases such as hypertension, cardiovascular-renal disease, gallbladder disease, anemia, diabetes, gastric ulcer, or generalized arteriosclerosis. In many instances, it is the drug that is the greatest offender in causing chronic or functional constipation in older patients whose senescent organism is undergoing the physiologic changes of aging.

Such drugs as antispasmodics, anticholinergics and hypotensive agents have a definite constipating effect. Some of these induce hypomotility in an intestinal tract which already has a slowed peristaltic action due to the aging process. Narcotics, for example, increase bowel atony (1). In this connection, it is of interest to consider how many narcotic drugs are consumed by the aged to relieve pain. Large or therapeutic doses of antibacterial agents disturb normal gastrointestinal physiology by altering the normal intestinal flora.

It is the consensus that the more powerful hypotensive drugs, such as the ganglionic blocking agents, cause marked restriction of bowel motility, leading to constipation (2–11). Moreover, ganglionic blocking agents are poorly absorbed from the intestinal tract; thus if constipation persists or becomes severe, a large and toxic amount of the drug may accumulate in the intestine, resulting in profound lowering of the blood pressure with all the possible sequelae (4, 5). Since large oral doses of these drugs must be given to be effective, it is important to check the bowel motility of patients receiving this therapy (3).

For example, it is imperative to include the use of laxatives in the therapeutic regimen of patients receiving pentapyrrolidinium (Ansolysen) or hexamethonium therapy (6, 11–13). A bowel movement should occur at least once every other day, else the medication must be stopped or the dosage greatly reduced. During prolonged therapy with such drugs, bleeding hemorrhoids may develop as a result of persistent constipation, necessitating discontinuance of treatment (5). Laxative foods and mild laxatives (cathartics if necessary) must be administered to avoid serious consequences (7), particularly in the elderly.

Drugs may even cause fecal impaction. Fecal impaction is frequent in the aged, especially in those who are inactive or bedridden. Medications such as kaolin, aluminum gels, calcium carbonate, bismuth salts and hygroscopic gums encourage the formation of excessive fecal masses and can result in impaction in

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an atonic bowel which may be unable to propel them. Impaction postoperatively is not infrequent (1).

With new drugs constantly appearing on the market for the treatment of a wide variety of diseases, constipation in the elderly may present an even greater problem than we realize. Only by clinical trial can we evaluate the side-effects of these medications, and it may be some time before we discover that one of the chief side-effects of a drug can be constipation or fecal impaction.

With the aging process and the wear and tear due to the habitual use of cathartics over a long time, gentleness should be the keynote in treating the elderly for constipation. We must be cognizant of the fact that we are dealing with patients who are usually taking some medication, and that the medication itself may be the precursor of constipation. By prescribing a mild, gentle laxative routinely, as a dietary management, we can thus avoid the constipating or hypoperistaltic effects of certain other drugs on an already hypotonic colon.

ETIOLOGY OF CONSTIPATION IN THE ELDERLY

According to Hurst (14), senile constipation is due chiefly to atonic dilatation and deficient peristalsis of the colon, resulting from atrophy of its musculature. Contributory factors may be the smaller quantity of the stool and the bland character of the food taken by older persons. Defecation is also less efficient, as the voluntary muscles which help in producing defecation share the senile atrophy of the muscles of the body, which is partly due to the sedentary life of the elderly.

Thewlis (15) attributes constipation in the elderly to a diminished capacity of the stomach and intestines, partly due to thickened mucous membranes and partly to lack of nourishment from arterial changes. The muscular coat of the intestines is atrophied, and impairment of function of the muscular coat, together with impaired peristalsis, contribute to intestinal atony. Constipation and diminished nutrition of the body result.

Atonic constipation is often found in inactive older persons and in those who have used cathartics and enemas over a period of years. The spastic type is characterized by hard, lumpy stools.

FREQUENCY OF CONSTIPATION IN OLDER PATIENTS

That elimination is one of the major problems accompanying advancing years is substantiated by the finding that more than half of geriatric patients take laxatives frequently (10, 11). In a recent survey of the diets of 100 persons 65 years of age or older, it was found that laxatives were taken routinely by 55 per cent, varying from three times a month to once or more daily (13, 16).

Portis and King (17) reviewed 133 ambulatory patients over 60 who had no organic abnormality to account for their symptoms, and found that 80 had symptoms referable to bowel habits. Of these, 41 had persistent constipation.

Sorter, Berg and Necheles (18) reported that constipation was one of the most frequent complaints in their patients above 60 years of age, and one of the most vexing problems therapeutically. All of their patients showed a lack of tone and contractile power of the sigmoid flexure and rectum.

The longer the laxative habit has been established in the elderly, the more dependent is the musculature upon irritants for stimulation, and the more difficult it becomes to re-establish normal muscle tone and activity. It takes time for the colon to "unlearn" its undesirable dependence upon irritants for stimulation. All laxatives are irritants, and increased peristalsis is a protective response. The enema habit or regular colonic irrigations induce similar consequences and should be considered in the same manner (1).

SIMPLE, DIETARY MANAGEMENT OF CONSTIPATION

After organic causes of constipation have been ruled out in the elderly patient, and a diagnosis of functional constipation has been made, the stools should be made soft and bulky by dietary management (19). Many elderly patients are on a therapeutic regimen for a prolonged period, as in the treatment of hypertension, cardiovascular disease, or urinary-tract infections. Therefore, a mild, dietary laxative should be prescribed that can be given over long periods without producing side-effects. The transition from dependency upon cathartics to normal bowel function is important, and the patient must be "educated" in breaking the laxative habit.

In the search for a laxative on the basis of mildness of action, and one that could be used for an indefinite period of time, a neutralized, non-diastatic barley malt extract (Malt Soup Extract[1]) was chosen because it acts on the basis of restoring normal physiology of the intestinal tract. This product acts by promoting favorable aciduric intestinal flora. It has been used for many years in correcting constipation in infants. In recent years it has been used clinically, with good results, in constipated elderly patients. Cass and Frederik (20) found that it produced soft, easily evacuated stools without any side-effects in constipated elderly patients. Marshall (21) found it a simple but highly effective treatment for chronic constipation in patients of all ages.

Clinical Observations

This dietary malt-extract regimen was tried clinically in 25 selected geriatric patients for the relief of drug-induced constipation. The ages of the patients varied from 54 to 86 years. All were receiving some form of drug therapy (hypotensive drugs, antispasmodics, antacids, insulin, bile salts, sedatives or narcotics), and all of them had been taking laxatives (mineral oil, cathartics, bulking agents, or enemas) for chronic constipation of approximately ten years' duration (Table 1). Malt Soup Extract was prescribed routinely, together with the patient's medication. The dosage varied from 1 tablespoonful three times daily to 2 tablespoonfuls twice a day. The consistency of the stools became soft in all patients and, within one week, bowel evacuations were accomplished with ease. Most patients liked the taste of the product, and the majority of them reported a feeling of well-being (Table 2). The following are typical case histories:

Case 1. Mrs. C. F., aged 58, who had essential hypertension for eight years, had a slight stroke. There was also a history of an acute coronary attack. Although she took various

[1] Borcherdt Malt Extract Co., Chicago, Ill.

TABLE 1

Drug-Induced Constipation in Geriatric Patients

Patient No.	Age (yrs.)	Sex	Diagnosis	Drug Therapy	Self-Prescribed Laxation for Constipation				
					Min. Oil	Irrit. Cath.	Bulking Agents	Salts	Enemas
1	59	F	Malignant hypertension	Reserpine; Ansolysen	√				√
2	69	M	Coronary heart disease	Digitalization	√				√
3	58	M	Diabetes mellitus	Insulin	√	√		√	√
4	74	F	Coronary heart disease; gallbladder disease	Digitalization		√			√
5	54	F	Coronary heart disease; essential hypertension	Reserpine; Ansolysen		√			
6	73	F	Duodenal ulcer	Antispasmodics; antacids		√	√	√	
7	68	F	Hypertension (malignant)	Reserpine; Ansolysen	√	√	√		
8	72	F	Hypertension (malignant)	Reserpine; Ansolysen	√	√	√		
9	74	M	Coronary heart disease with decompensation	Digitalization	√			√	√
10	74	M	Cardiac disease	Digitalization	√	√		√	√
11	74	F	Ulcerative colitis	Antispasmodics; antacids	√		√		√
12	58	M	Duodenal ulcer; gallbladder disease	Antacids; bile salts; antispasmodics & sedatives	√				√
13	86	M	Hypertensive heart disease	Digitalization; sedation	√	√			
14	82	F	Arteriosclerosis; hypertension (severe)	Reserpine; Ansolysen	√		√		
15	69	F	Chronic coronary disease with decompensation	Digitalization; sedation		√			
16	71	F	Gallbladder disease	Antispasmodics; bile salts	√				
17	64	M	Hypertensive heart disease	Nitranitol with Rauwolfia; digitalization			√		
18	57	F	Atonic bowel; colitis	Antispasmodics; antacids	√	√	√	√	√
19	75	M	Arteriosclerosis	Reserpine; Ansolysen	√		√		√
20	54	M	Cardiac disease	Digitalization; sedation	√		√	√	√

TABLE 1—*Continued*

Patient No.	Age (yrs.)	Sex	Diagnosis	Drug Therapy	Self-Prescribed Laxation for Constipation				
					Min. Oil	Irrit. Cath.	Bulking Agents	Salts	Enemas
21	72	F	Hypertension (malignant)	Reserpine; Ansolysen	√	√		√	√
22	81	M	Arteriosclerosis; hypertension	Reserpine; Ansolysen	√	√	√	√	
23	69	M	Hypertension (malignant)	Reserpine; Ansolysen	√	√	√		√
24	76	M	Arteriosclerosis; psychosis	Reserpine; Ansolysen	√		√	√	
25	63	F	Diabetes mellitus; coronary disease; hypertension	Insulin; reserpine; Ansolysen	√	√			√

vasodilators and hypotensive drugs for seven or eight years, she did not respond until Ansolysen was prescribed. After taking Ansolysen for several days, severe constipation developed. Malt Soup Extract was advised for her constipation. Her bowel movements became normal.

Case 2. R. H., a woman aged 73, was under treatment for duodenal ulcer for about thirty years. At the time of observation, she had been taking antacids and antispasmodics for three years. Severe constipation with impaction had developed. As she was taking increased amounts of aluminum hydroxide, her constipation became worse. Under treatment with Malt Soup Extract, her stools became softer, and her bowel movements more frequent and normal.

Case 3. Mrs. M. G., aged 71, had had coronary heart disease for about eight years, with gallbladder dyskinesia. She complained frequently of dyspepsia, eructations, gas, bloating and difficulty in bowel movements. After cardiac compensation had been established and Malt Soup Extract prescribed, her gallbladder symptoms disappeared and her bowel movements became normal.

In general, cathartics should be avoided, or should be reserved for cases in which they may be indicated temporarily, such as in the postoperative period or following cerebrovascular accidents. Cathartics should be used only to reactivate bowel movements, and should be followed by the milder dietary management (19).

Table 3 contains a summary of the salient points concerning the mode of action of the various cathartics discussed by Goodman and Gilman (22). It will be noted concerning all the cathartics described, that they either have unfavorable effects or they should be given with certain reservations. In the case of mineral oil, it is well established in the literature that this oil should not be given over prolonged periods because of interference with vitamin absorption. Morgan (23), in pointing out the disadvantages of the use of mineral oil, states that it makes a complete evacuation impossible. It may prevent postoperative healing of rectal wounds, and may be an indirect factor in pruritus ani. Moreover, it has been demonstrated in animals that liquid petrolatum is absorbed from the gastrointestinal tract and is deposited in the liver (24). It

TABLE 2

Management of Geriatric Constipation with Malt Soup Extract

Patient No.	Initial Dose			Maintenance Dose							Administration						Results		
	2 Tbs.* t.i.d.	Days	Wks.	1 Tbs.	2 Tbs.	Once a day	b.i.d.	t.i.d.	Mos.	Yrs.	With meals	At bedtime	By spoon	Milk	Fruit juice	Coffee	Stools soft (days)	Frequency satisfactory	Constipation relieved
1	✓		2	✓				✓	3		✓	✓	✓				3	✓	✓
2	✓		1	✓				✓	16		✓	✓	✓				2	✓	✓
3	✓		1	✓			✓		10		✓	✓	✓				7		✓
4	✓	10		✓				✓	6		✓	✓	✓	✓			8–10	✓	✓
5	✓	3		✓				✓		2	✓	✓	✓		✓		3	✓	✓
6	✓	1			✓	✓				3		✓	✓	✓			2	✓	✓
7	✓	5			✓		✓		8		✓	✓	✓		✓		5	✓	✓
8	✓	5			✓		✓			4		✓	✓	✓			5		
9	✓	7		✓				✓		1	✓	✓	✓	✓			7	✓	✓
10	✓	3		✓			✓			1	✓	✓	✓		✓		3	✓	✓
11	✓	8		✓				✓		2	✓	✓	✓	✓			8	✓	✓
12	✓		2		✓	✓				4		✓	✓				8	✓	✓
13	✓	5			✓		✓		8		✓	✓	✓		✓		5	✓	✓
14	✓	7		✓			✓		5		✓	✓	✓		✓		7		✓
15	✓	4		✓				✓		2	✓	✓	✓	✓			4	✓	✓
16	✓	6		✓			✓			3	✓	✓	✓			✓	6		✓
17	✓	12		✓			✓			3	✓	✓	✓	✓			12		✓
18	✓	6		✓			✓		3		✓		✓		✓		3	✓	✓
19	✓	5			✓		✓			3	✓	✓	✓	✓			5	✓	✓
20	✓	7			✓	✓			6			✓	✓	✓			7	✓	✓
21	✓	8		✓			✓			1	✓	✓	✓				8	✓	✓
22	✓	10		✓				✓		3	✓	✓	✓				8		✓
23	✓	5		✓		✓				3		✓		✓					
24	✓	12		✓			✓			2	✓	✓	✓				10	✓	
25	✓				✓		✓			4	✓	✓				✓	8	✓	

* Tablespoonful.

TABLE 3

*Action of the More Important Cathartic Drugs**

Cathartic	Mode of Action	Remarks
Emodin		
Cascara sagrada	Acts only on large intestine; therefore delayed action (8–24 hrs.).	Excreted products may color urine. Long-term use may produce pigmentation of rectal mucosa.
Senna	More active than cascara; acts usually in 6 hrs.	Causes considerable griping.
Rhubarb	Acts in 4–6 hrs.	Tannin content has astringent action. Evacuation may be followed by constipation.
Aloe	Most irritating of emodin drugs; delayed action (8–12 hrs.).	Causes considerable griping and pelvic vascular congestion. Excessive doses may cause nephritis.
Irritant oil		
Castor oil	Irritant to small intestine; causes rapid evacuation. Semi-fluid stools within 2–6 hrs.	Little griping.
Miscellaneous		
Phenolphthalein	Greatest effect on colon; effect also on small intestines. No significant irritation.	Pleasant to take. Nontoxic except for idiosyncrasies (may cause excessive purgation, skin rashes in hypersensitive patients). Colors alkaline urine or feces.
Mercurous chloride calomel	Converted to mercuric oxide, which is extremely irritating to intestinal tract. Semi-fluid stool within 12 hrs.	Rarely indicated, because of potential danger. If no effect is obtained after 10 hrs., a saline cathartic must be given to eliminate the toxic mercury from the intestines.
Saline	Basic principle of action of all saline cathartics is to attract water by osmotic pressure of retained salt ions. Action may be likened to that of an enema, due to resultant fluid accumulation in the colon.	Because saline cathartics attract fluid into intestines, they may lead to dehydration.
Magnesium sulfate (Epsom salt)	As above	Accumulation of Mg ions may cause intoxication. Contraindicated in renal disease.
Milk of magnesia (magnesia magma)	As above	Better antacid than cathartic. Cathartic dose contains little more than 1 Gm. of magnesium hydroxide and thus cannot retain much fluid in GI tract.
Magnesium citrate	As above	Expensive, but pleasant saline cathartic.
Sodium sulfate (Glauber's salt)	As above	One of cheapest and most effective saline cathartics.

* Tablespoonful.

TABLE 3—*Continued*

Cathartic	Mode of Action	Remarks
Saline (*continued*)		
Sodium phosphate	As above	Pleasant-tasting saline cathartic.
Potassium and sodium tartrate (Rochelle salt; Seidlitz powders)	As above	Powders to be taken together (2.5 Gm. sodium bicarbonate and 7.5 Gm. Rochelle salt).
Colloidal and fibrous		
Bran	Fiber content increases bulk of intestinal contents.	Large amounts necessary for cathartic effect.
Agar	When moistened, agar swells and forms a mucilaginous mass, increasing bulk.	Large amounts necessary for good effect.
Psyllium seed	Seeds swell in bowel to form emollient indigestible mass.	Seeds should be swallowed whole, since they contain a pigment which is excreted through the kidney. Large amounts of water necessary to avoid swelling in the esophagus and consequent obstruction.
Emollient		
Liquid petrolatum (white mineral oil)	Acts as a lubricant of feces, since it is not absorbed.	Retards gastric emptying time. Not to be taken with meals. Large doses may leak through anus and cause pruritus ani. Questionable if mineral oil can be used safely over long periods of time. Indiscriminate use by elderly should be discouraged.

* Adapted from Goodman, L. S., and Gilman, A. (22).

may leak from the rectum, carrying carotene with it, and stain the clothing. Bulking agents may result in intestinal impaction or obstruction, and even ruptured bowel, especially in older patients who have a chronic diverticulitis. Saline cathartics produce watery stools, then permit a swing back to hard, dry stools. All of these agents, therefore, are undesirable in geriatric patients whose intestinal tract is undergoing the aging process, particularly when a laxative must be given for a long and indefinite period of time. It seems desirable, therefore, that geriatric constipation, particularly if drug-induced, should be corrected by a substance that has a mild, yet effective, physiologic mode of action.

SUMMARY

Constipation in elderly patients is common. Treatment requires special care. The colon is often weakened by the aging process and by the habitual use of

laxatives. Constipation is often due to drugs, such as the more powerful hypotensive agents. Accumulation of such drugs in the intestines, due to constipation, is dangerous and should be avoided. Saline cathartics, mineral oil, and bulking agents have specific disadvantages, especially in geriatric patients requiring medication over a long period of time. In these patients, gentle laxation without side-effects is important in the treatment of constipation. A neutralized non-diastatic barley malt extract[1], a dietary preparation with gentle, physiologic stool-softening properties, was used clinically in 25 selected cases of geriatric constipation due to drug therapy. Constipation was relieved without side-effects and progress was made in restoration of normal bowel action. This extract can be taken for an indefinite period of time without producing any pathologic changes (anatomic or physiologic) in the intestinal tract.

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RELIEF OF NOCTURNAL LEG CRAMPS—STROKE PREVENTION?

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In a previous article (1) it was suggested that methoxyphenamine (Orthoxine) hydrochloride may offer some protection against the formation of thrombi by improving arteriolar circulation. A review of results in a group of geriatric patients receiving this compound regularly has been made in an attempt to evaluate its possibilities.

Methoxyphenamine has been the drug of choice in my practice during the past five years for the relief of nocturnal leg cramps. This is a frequent complaint, and often the presenting one, among the elderly. Usually the cramps awaken the patient after an hour or more of sound sleep. They are relieved by rubbing the leg muscles or by walking about. The pathologic lesion involved is sclerosis and partial occlusion of arteriolar circulation, usually with generalized arteriosclerosis. Methoxyphenamine at bedtime prevents occurrence of cramping by a prolonged (four to six hours) inhibition of smooth muscle spasm. A dose of 100 milligrams has been found effective in 196 of 200 patients over 55 years of age. Three of this group required repetition of the dose. One responded to only 50 mg., experiencing undue psychomotor stimulation at full dosage.

Another older group of patients was chosen for this study, in order to evaluate the protective influence of the drug against vascular complications in arteriosclerosis. It is apparent that a person who has arteriosclerosis severe enough to cause nocturnal leg pains, has received nature's physiologic warning, and probably has sclerosis of vessels elsewhere in the body. These are the patients who so often are afflicted with strokes—coronary or cerebral thromboses. Many of these strokes are obviously associated with extremes of weather, which provoke vascular changes in these people that may exceed their tolerance or safety threshold. More strokes occur during acute cold spells, stormy autumns, extremely cold winters, and overbearingly hot periods of the year. There is a certain correlation with nocturnal leg cramps, which may occur on frosty and cold nights but not on warm spring and summer nights. Customarily, therefore, methoxyphenamine therapy is omitted during the spring and summer months and restarted in the fall.

CLINICAL OBSERVATIONS

All patients over 65 years of age at the onset of therapy were included in this survey. They totaled 164, ranging in age from 65 to 92 years, with an average of 73. All had definite signs of arteriosclerosis, in addition to being afflicted with leg cramps. Most were also under treatment for other diseases such as hypertension, congestive heart disease, pellagra and various nutritional deficiencies, diabetes, carcinoma, varicosities, dermatitis, prostatism, cerebral arteriosclerosis or coronary artery disease. Many had had several cerebral thromboses already.

Several had already survived coronary infarcts. The average duration of treatment in this series was 24.6 months, varying from three to sixty months. Occasionally the patients felt so much better while receiving therapy that they discontinued it, not realizing that their pathologic circulatory condition remained essentially unchanged, though functionally improved. In this series there were 7 such patients who died after discontinuing treatment. Most of these reportedly had strokes, but no accurate diagnosis was available. However, it was these cases that sharpened the suspicion that methoxyphenamine might be protecting its users from a similar fate.

There were 5 deaths in patients while under treatment:

1. Age 68, diabetes, congestive heart failure.
2. Age 75, carcinomatosis.
3. Age 71, diabetes, cerebral hemorrhage and hypertension.
4. Age 82, arteriosclerotic heart disease with auriculoventricular block, and a probable infarct.
5. Age 77, cerebral thrombosis.

There were no other known episodes of cerebral thrombosis, and no coronary thromboses in this group while under treatment. All patients were seen once a month, or more often if necessary. The total was 336.3 patient-years of therapy, or an average of 24.6 months each. This places the incidence of coronary death, cerebral thrombosis, and cerebral hemorrhage each at approximately 0.3 per cent per year. Annual case rates per thousand population for cerebral hemorrhage, embolism, and thrombosis, in persons aged 65 and over, have been given as 28.21 (2). Further and more exacting work on this problem may reveal the statistical significance of the results with this drug.

SUMMARY

Methoxyphenamine (Orthoxine) hydrochloride has been found effective in preventing leg cramps in 164 patients, aged 65 to 92 (average age, 73).

It is suggested that this drug may have prevented vascular complications in these patients, as indicated by an annual incidence of about 0.3 per cent each for cerebral thrombosis, coronary death, and cerebral hemorrhage.

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LETTER TO THE EDITOR

ETOPALIN: A NEW SUBSTANCE USEFUL FOR PRODUCTION OF FOCAL INTRACEREBRAL LESIONS IN HUMAN SUBJECTS

To The Editor:

In March 1954, a simple technique was described (1) for direct intracerebral procaine injection into the region of the globus pallidus in hyperkinetic disorders. This technique was extended during the subsequent year so that the procaine injection into the globus pallidus was followed by an intracerebral alcohol injection. The alcohol, when injected directly into the mesial globus pallidus, produced a lasting alleviation of contralateral tremor and rigidity in parkinsonian patients (2). This latter technique, which was named chemopallidectomy, has now been utilized in a series of more than 200 patients. It can alleviate parkinsonian tremor and rigidity in at least 70 per cent of properly selected patients. The mortality rate, up to the present time, is 3 per cent.

During the development of chemopallidectomy it became apparent that the intracerebral injection of absolute alcohol was attended by certain risks which were inherent in the nature of the neurolytic substance being injected into the brain. The greatest risk involved in the use of absolute alcohol during this procedure was the possibility of the spread of this substance to adjacent intracerebral structures other than the globus pallidus. It was conjectured that if the alcohol could be made more viscous it would have less tendency to spread into adjacent areas or nerve-fiber planes, and would thereby be more useful for production of a focal intracerebral lesion. At our request, such an agent has been developed by Ciba Pharmaceutical Products Inc. It has been employed by us during the past year in 100 cases of chemopallidectomy. It is the purpose of this report to call attention to this new neurolytic agent—as an addendum of the technical article appearing in this Journal in November 1955 (3).

Etopalin is an 8 per cent solution of a specially prepared cellulose in 95 per cent ethyl alcohol, adapted for intracranial administration. The method of preparing the solution involves the addition of ethyl cellulose to ethyl alcohol, accompanied by thorough mixing to insure complete solution and proper viscosity. Sterilization is accomplished by standard U.S.P. techniques.

Intracerebral injections of Etopalin have been carried out in a series of 100 animal experiments (4). These have demonstrated that, when slowly injected, this substance is capable of producing a uniform, circumscribed, oval shaped, neurolytic lesion. It is unattended by cerebral edema or other undesirable pathologic effects. Etopalin has also been used in a consecutive series of 100 cases of chemopallidectomy in patients with parkinsonism. It has been eminently satisfactory, as judged by clinical results, for the production of a focal, neurolytic lesion in the globus pallidus in these cases. Etopalin has also been employed for the production of small, focal lesions in the frontal lobes in certain cases of selective lobotomy. Its efficacy in this instance has also been noteworthy. It is

my opinion that Etopalin is the best substance currently available for use in chemopallidectomy and that it may deserve wider employment as a neurolytic agent in neurologic surgery.

IRVING S. COOPER, M.D.*

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Abstracts of Current Literature

PRIMARY MELANOMA OF THE FEMALE URETHRA.

Abrams, M. *J. Urol.* **74:** 371 (Sept.) 1955.

The fifteenth case of primary melanoma of the female urethra is presented. The tumor was excised. At eighteen and twenty-seven months, respectively, thereafter metastatic inguinal lymph nodes were removed. The patient is alive and asymptomatic. Melanoma has been variously referred to as melanocarcinoma, nevocarcinoma, melanoepithelioma, melanosarcoma, and malignant melanoma, perhaps because of uncertainty as to its origin. Its origin from nerve tissues is the favored theory. The microscopic characteristics are described. It is found in older age groups. Frequency and burning on urination have been the only urinary symptoms recorded. In many of the first 14 patients with urethral melanoma, the first symptoms were the presence of a vaginal tumor and a foul-smelling serosanguinous vaginal discharge. The melanoma usually occurs in the distal portion of the urethra. Its color varies, and this variance emphasizes the importance of preserving all tumors of the urethra for microscopic study. In the differential diagnosis, caruncle, carcinoma, sarcoma, fibroma, chancre, and prolapsed mucosa must be excluded. Melanoma is radioresistant and the prognosis is extremely poor. Metastasis to the inguinal nodes or skin occurs early. Treatment has been generally unsatisfactory, and there have been no five-year survivals.

THE BLOOD VOLUME IN CANCER.

Berlin, N. I.; Hyde, G. M.; Parsons, R. J., and Lawrence, J. H. *Cancer* **8:** 796 (July–Aug.) 1955.

The blood volume was determined in 66 patients with cancer of various tissues, using a modified Hevesy and Zerahan method with P^{32}-labeled red blood cells. Patients having a total red cell volume of less than 24 cc. per Kg. of body weight were classified as anemic. By this criterion, 31.8 per cent of the patients were anemic. Of the anemic group, 76.2 per cent had metastases, and the percentage in the nonanemic group was approximately the same. The mortality rates in both groups were also approximately equivalent. In 67 per cent of the patients with anemia, there was hemorrhage, cachexia, or infection, alone or in combination. The cause of the anemia occurring in cancer in the absence of hemorrhage, infection, or cachexia is not clear, but a possible mechanism is an abnormally short red-cell life span, similar to that seen in leukemia.

INFLUENCE OF AGE AND VASCULAR DISEASE ON CEREBRAL HEMODYNAMICS AND METABOLISM.

Fazekas, J. F.; Kleh, J., and Finnerty, F. A. *Am. J. Med.* **18:** 477 (March) 1955.

The influence of aging, hypertension and focal or generalized cerebrovascular disease on cerebral hemodynamics and metabolism was determined, and the results compared with those of other investigators. Most authors agree that aging is associated with a significant decrease in the rate of cerebral blood flow, a fall in the cerebral metabolic rate and a significant increase in cerebrovascular resistance. These changes are most likely due to a progressive increase in the degree of cerebral arteriosclerosis with age. Significant reductions in the rate of cerebral blood flow from values found in normal young subjects may occur in elderly subjects, acutely and chronically, without a significant change in cerebral oxygen utilization and without obvious impairment in the functional activity of the higher centers. Essential

hypertension in both young and elderly subjects is invariably associated with increased cerebrovascular resistance. In elderly subjects this increased resistance is due in part to cerebral arteriosclerosis. In subjects with essential hypertension without overt evidence of cerebrovascular insufficiency (focal or generalized), the rate of cerebral blood flow and oxygen utilization is not significantly different from values noted for subjects of a similar age range without hypertension. Cerebrovascular insufficiency may occur earlier in subjects with hypertension but the reduction in cerebral blood flow and metabolism is not of greater magnitude than that noted for normotensive subjects with similar disturbances. These results suggest that hypertension may well be an accelerating factor in the production of cerebrovascular disease, but is not necessarily etiologic. In elderly subjects with psychosis (senile or cerebral arteriosclerosis, or both) with or without hypertension and no focal evidence of cerebrovascular insufficiency, a significant reduction of cerebral blood flow and cerebral oxygen consumption was noted. It cannot be concluded with certainty that the mental deterioration in such subjects is a consequence of the decreased delivery of essential substrates. (From authors' summary and conclusions.)

THE POSSIBLE SIGNIFICANCE OF A T-WAVE VARIANT AS DETERMINED FROM ITS AGE DISTRIBUTION AND PREVALENCE PRIOR TO MYOCARDIAL INFARCTION.

Fritz, W. F., and Sjoerdsma, A. *Am. Heart J.* **50:** 203 (Aug.) 1955.

An attempt has been made to determine the significance of anteriorly directed mean T-forces in the electrocardiogram as manifested by low T waves on the limb leads, isoelectric or slightly inverted T waves at V_5 and V_6, and upright T waves at V_1 to V_4, with normal QRS. A prevalence study was made of this T-wave variant in the electrocardiograms of three groups of patients: 1) a control group of 700 men in the Armed Forces, 2) 272 males over the age of 60, and 3) 95 patients in whom electrocardiograms had been taken at least one month prior to the development of myocardial infarction. The prevalence of this T-wave pattern in the elderly and pre-infarct groups was significantly greater than in the control group, as determined by statistical analysis. This was felt to constitute presumptive evidence that the pattern, in some instances, may be the earliest sign of left ventricular ischemia, occurring even before clinical symptoms become manifest. This electrocardiographic syndrome is deserving of further critical appraisal and long-term evaluation to determine its prognostic significance in the otherwise normal individual. (From authors' summary.)

SOME BEHAVIORAL EFFECTS ASSOCIATED WITH FEEDING SODIUM GLUTAMATE TO PATIENTS WITH PSYCHIATRIC DISORDERS.

Himwich, H. W.; Wolff, K.; Hunsicker, A. L., and Himwich, W. A. *J. Nerv. & Ment. Dis.* **121:** 40 (Jan.) 1955; through *Digest Neurol. & Psychiat.* **23:** 267 (June) 1955.

Twenty-seven patients between the ages of 50 and 76 years, with different types of schizophrenic reaction, various forms of brain syndrome, and (in 1 instance) psychoneurosis, were studied over an eleven-month period. Following initial administration of placebo, the patients were divided into two groups. Each received alternately placebo or sodium glutamate for two successive experimental periods, and was observed for an additional period free of supplement of either type. Statistical analyses of the results of perceptual and motor coordination tests failed to disclose any significant changes associated with glutamate feeding. The basal metabolic rate, EEG, ECG, pupillary dilatation, blood pressure, heart rate, respiratory rate, oral temperature, and body weight underwent no consistent alterations as a result of the medication. Seventeen of the 27 patients receiving monosodium glutamate improved clinically, 16 in action, 12 in emotion, 9 in intellection, 8 in interpersonal relationships, 5 in thought processes, and 2 in insight. The behavior in 8 patients remained unchanged and in 2 became worse. The improvement was maintained for some time after the drug was withdrawn. Nine patients received the drug for two periods; the

dosage during the first period was 15 Gm. daily and during the second, 45 Gm. daily. Two of these patients did better when taking 45 Gm. and 1 did better when taking 15 Gm. The other 6 patients showed the same degree of improvement with each dosage. A dosage of 15 Gm. as the monosodium salt was concluded to be adequate and unlikely to be accompanied by unpleasant side-actions. With this amount, administered three times daily, the blood level was raised above normal for periods of half a day or less. It was found that a possible cause for discrepancies reported in the literature concerning the action of glutamic acid may have been the administration of glutamic acid in three forms: glutamic acid hydrochloride, glutamic acid, and sodium glutamate—compounds not equally absorbable into the blood stream.

COMBINED HYDROGENATED ALKALOIDS OF ERGOT IN MENTAL AND NERVOUS DISORDERS ASSOCIATED WITH OLD AGE.

Hollister, L. E. *Dis. Nerv. System.* **16:** 259 (Sept.) 1955; through *Digest Neurol. & Psychiat.* **23:** 471 (Oct.) 1955.

Determination of the effects of Hydergine (a mixture of equal parts of dihydroergocornine, dihydroergocristine, and dihydroergokriptine) was undertaken in patients hospitalized with psychoses associated with old age. The 26 patients ranged in age from 56 to 83 years. On the basis of chance selection, they received either Hydergine or identical-appearing placebo tablets. The dosage schedule was as follows: two tablets (1 mg.) sublingually four times daily for thirty days, two tablets three times daily for fifteen days, and two tablets twice daily during the last fifteen days. Each patient's mental and physical status was carefully assessed before, and immediately after the study. The Hospital Adjustment Scale was used for the evaluation of behavioral changes. Eight of the 13 patients who received Hydergine improved, whereas only 1 of those who received placebos improved. Unequivocal improvement in behavior and mental state was produced in 2 patients with chronic brain syndromes due to hypertension. The first patient, who was ordinarily irritable, disinterested, and moderately confused, became alert, sociable, and uncomplaining during treatment. The second patient, who prior to treatment had many paranoid delusions, became friendly and sociable, while delusions and ideas of reference decreased. Hydergine was concluded to be beneficial in patients with hypertensive brain disease because of its ability to lower blood pressure and vascular resistance in the cerbral vessels. None of the patients experienced adverse effects. The blood pressure decreased slightly in most of those who received Hydergine, but in none did it fall below physiologic limits. The drug caused no striking amelioration in the mental or nervous symptoms of chronic brain syndromes due to senile, arteriosclerotic, or traumatic brain disease. However, it was subsequently found to be of considerable value in the treatment of a patient with an acute brain syndrome due to hypertension and in a patient with an acute cerbrovascular accident. In the latter patient, hemiplegia was nearly completely relieved, the result being comparable to the best results obtained from the use of cervical sympathetic block. Hydergine would appear to be indicated in these conditions, if hemorrhage is first ruled out.

AFFECTIVE DISORDERS ARISING IN THE SENIUM. I. THEIR ASSOCIATION WITH ORGANIC CEREBRAL DEGENERATION.

Kay, D. W. K.; Roth, M., and Hopkins, B. *J. Ment. Sci.* **101:** 302 (Apr.) 1955; through *Digest Neurol. & Psychiat.* **23:** 406 (Sept.) 1955.

Results of previous investigations support the authors' hypothesis that affective disorder in old age is a separate nosologic entity. Although affinities exist between old-age affective disorder and manic depressive and other functional affective illnesses of earlier life, it was thought that there was a possibility that an organic factor in the etiology of the group of late onset was concealed by dilution with cases in which this was unlikely to appear. The authors therefore studied 189 patients with a manic or depressive symptom complex of at least a few weeks' duration, in order to determine the possible part played by organic

cerebral degeneration in affective disorders arising in the senium. Of 175 patients with affective disorder proper, 89 had had their first attack at the age of 60 or later, and 86 before the age of 60. Of 14 showing a mixed symptomatology consisting of a variable depressive mood change and sometimes typical depressive ideation in a clear organic setting, 5 belonged to the early and 9 to the late onset group. The early and late onset groups were compared with respect to clinical signs of organic nervous system disease and cerebral involvement, psychometric test results, and outcome. Comparing the symptomatology and mental test performance, two groups with affective disorder did not differ in frequency of signs of cerebral involvement. Both differed significantly from the organic psychoses to which the mixed cases tended to conform. Although patients in both groups are exposed to some risk of cerebrovascular disease in old age, the risk is probably no greater than in the normal population. The slightly larger number of patients with cerebrovascular symptoms found in follow-up of the late onset group was probably due to the higher mean age. However, further study is indicated. The pattern of outcome was similar for the two groups, with the majority discharged and few dead—a different pattern from that of organic psychotics. The slightly greater mortality of the late onset group represented a real, although not significant, difference associated with the higher incidence of physical illness in this group. "Mixed" cases had a far worse prognosis; 2 of these patients were discharged and 7 died. The data suggest that cerebral degeneration of the kind found in senile and arteriosclerotic psychoses is not contributory to causation of affective psychosis in late life, whether or not the latter first appears in the senium. Appearance of affective disorder for the first time in old age rather suggests a postponement of the manifestation of a predisposition to mental illness. Depressive or manic psychosis of late onset and affective disorders of earlier life form a nosologic entity distinct from psychoses with cerebral degeneration.

MALIGNANT LYMPHOMA OF THE THYROID APPARENTLY ARISING IN STRUMA LYMPHOMATOSA.

Kenyon, R., and Ackerman, L. V. *Cancer* **8:** 964 (Sept.–Oct.) 1955.

Examination of the marginal thyroid tissue in 2 cases of malignant lymphoma of the thyroid showed changes consistent with struma lymphomatosa. In both cases the portion of the thyroid not replaced by the neoplasm showed the small colloid-poor acini formed by plump, acidophilic epithelial cells. The acini were arranged in small clumps and were surrounded by broad zones of lymphocytes forming prominent follicles. These changes were universal, and consistent with a diagnosis of struma lymphomatosa. The pattern of malignant lymphoma was demonstrated by sheets of lymphoid cells invading the surrounding tissue. The tumor in each patient presented primarily in the thyroid. Both patients had a history indicative of thyroid disease prior to the development of malignant lymphoma. The course of the disease is rapid and these patients died from the neoplasm in less than a year. One conclusion that might be drawn from these findings is that the foregoing changes are involved in the histogenesis of some of the thyroid lymphomas. Malignant lymphomas may arise from the lymphoid tissue which is present in a wide variety of thyroid disease. Adequate examination of the marginal, uninvolved portion of the thyroid gland may reveal evidence of the antecedent disease.

LEVARTERENOL BITARTRATE (LEVOPHED) IN THE TREATMENT OF CARDIAC ARRHYTHMIAS.

McGinn, J. T., and Schluger, J. *Am. Heart J.* **50:** 625 (Oct.) 1955.

Six cases of supraventricular paroxysmal tachycardia and 1 of ventricular tachycardia are presented, in which termination of the attack was brought about by the administration of levarterenol intravenously in a concentration of 8 to 16 mg. per 1,000 cc. of 5 per cent glucose in water at the rate of 20 to 40 drops per minute. In a case of auricular flutter, the rate was temporarily slowed but the abnormal rhythm persisted. Administration of the

drug was successful only when it elevated the blood pressure to approximately normal levels. It is suggested that levarterenol acts in cases in which it causes reversion to normal rhythm by elevating the blood pressure. This stimulates receptors in the aorta and carotid sinus, causing reflex stimulation of the vagus. The profound vagal stimulation thus induced causes cessation of the attack. Levarterenol appears to be a safe, efficacious means of treating paroxysmal tachycardia. No deleterious effects were noted.

THE RESULTS OF URETERAL TRANSPLANTATION TO A RECTOSIGMOIDAL POUCH.
Melick, W. F., and Naryka, J. J. *J. Urol.* **74:** 47 (July) 1955.

The literature on uretero-intestinal anastomosis is reviewed. The disadvantages of the various procedures are cited. Melick and Naryka describe the procedure for ureteral transplantation into the rectosigmoidal pouch with cystectomy and colostomy. It is easier and more quickly accomplished than other technics that have been described. It is applicable to cases of bladder carcinoma in which the rectum usually does not have to be sacrificed and it is possible to utilize the rectum and a small portion of the sigmoid to construct a substitute bladder. This technic was successfully used in 6 patients from whom the bladder was removed because of carcinoma. The use of the rectosigmoid pouch as a substitute bladder in these patients had the advantages that: urinary continence was preserved by using the rectal sphincter, urinary obstruction and infection were eliminated by the diversion of the fecal stream, and the danger of fecal fistula was eliminated. No hyperchloremic acidosis occurred except in a patient with pre-existing chronic pyelonephritis in whom there was incomplete emptying of the rectosigmoid. The only disadvantage to the procedure is the specialized daily care required for the colostomy.

MUCOUS ADENOCARCINOMA OF THE URINARY BLADDER.
Mostofi, F. K.; Thomson, R. V., and Dean, A. L., Jr. *Cancer* **8:** 741 (July–Aug.) 1955.

Data from 44 cases of mucous adenocarcinoma of the bladder taken from the Bladder Tumor Registry at the Armed Forces Institute of Pathology are presented. The patients ranged in age from 18 to 77 years. Hematuria was the most frequent symptom. The review shows that primary mucous adenocarcinoma may occur anywhere in the bladder. It tends to be infiltrating and its behavior resembles that of infiltrating transitional-cell carcinoma of the bladder. The five-year survival rate was 27 per cent and the five-year mortality rate about 70 per cent. The pathologic features of these tumors are given. Grossly the distinguishing characteristic was the presence of mucus on the external surface or in the substance of the tumor. Microscopically the characteristic feature was the presence of extracellular and intracellular mucus. Seventeen tumors that were probably urachal in origin were characterized clinically by a more unfavorable course. All except 3 of the patients died in less than five years. The poor prognosis may have been due to incomplete removal, as these tumors tend to spread along the remnants of the pre-existing urachal tract, not only in the bladder wall but also in the anterior abdominal wall. For primary vesical adenocarcinoma (excluding urachal adenocarcinoma), the five-year survival rate postoperatively without tumor was about 33 per cent, and the five-year tumor-free rate postoperatively was 25 per cent. In 2 instances, the bladder was exstrophic. Patients with exstrophy of the bladder should be carefully watched for the development of tumor if cystectomy cannot be performed at an early age. When the mucosa adjoining the tumor shows polypoid formation, Brunn's nests, and glandular and mucous metaplasia, the tumor is probably a primary vesical adenocarcinoma. Associated areas of transitional and squamous-cell carcinoma favor this diagnosis. The tumor is probably secondary if the adenocarcinoma is intramural, if the tissue is from an area of bladder other than the dome or the anterior wall, and if no change but ulceration appears in the mucosa. A similar tumor occurring in the dome or anterior wall may be urachal in origin. The latter may also show an admixture of

adenocarcinoma and transitional and/or squamous carcinoma. In differentiating between vesical and urachal adenocarcinoma, the presence of proliferative and so-called metaplastic changes in the noncancerous mucosa adjoining the tumor is considered indicative of primary vesical adenocarcinoma, whereas the absence of such changes would favor a diagnosis of urachal adenocarcinoma. Secondary tumors of the bladder rarely give rise to urinary symptoms before the primary site is detected. Evidence favors the theory that mucous adenocarcinoma of the bladder originates from the transitional epithelium of the bladder rather than from "enteric rests." The treatment of choice is complete removal of the tumor and control of infection. Total cystectomy is indicated only in certain patients. In the case of a malignant urachal tumor, the primary lesion must be removed and its extensions widely excised.

EFFECTIVENESS OF ARAMINE IN THE TREATMENT OF SHOCK.

Moyer, J. H., and Beazley, H. L. *Am. Heart J.* **50:** 136 (July) 1955.

Aramine (levo 1-(*m*-hydroxyphenyl)-2-amino-1-propanol) administered by constant intravenous infusion to 20 patients proved effective in restoring and maintaining blood pressure in clinical shock due to common causes. All of the patients probably would have died had not vasopressor therapy been available. On a weight basis, Aramine was less potent than norepinephrine, but in comparison with the latter substance it showed an advantage in that its action was less evanescent so that a more stable blood pressure could be maintained. No slough resulted from its use intravenously. Compromised renal function was improved, in that there occurred an increase in glomerular filtration rate, renal blood flow, and urinary output. The state of consciousness of the patients seemed to be improved when normal blood pressure was restored. Aramine administration was attended by a reduction in cardiac rate in all except 2 patients.

CLINICAL RESPONSE AND CHANGES IN NITROGEN BALANCE, BODY WEIGHT, PLASMA PROTEINS, AND HEMOGLOBIN FOLLOWING TUBE FEEDING IN CANCER CACHEXIA.

Pareira, M. D.; Conrad, E. J.; Hicks, W., and Elman, R. *Cancer* **8:** 803 (July–Aug.) 1955.

Clinical and metabolic evidence is presented to show that cancer cachexia is not due to any specific effects of cancer but to malnutrition initiated and sustained by anorexia. Hyperalimentation by tube feeding served to break the anorexia-malnutrition cycle in cachetic patients with advanced cancer and to induce weight gain and return of appetite, as well as positive nitrogen balance and regeneration of hemoglobin, as in non-cancer cachexia. Only in the regeneration of serum albumin did the cancer patient show a possible impairment. The method of tube feeding employed to provide hyperalimentation was clinically satisfactory and beneficial in the terminal care of selected patients with cancer cachexia. (From authors' summary.)

ACUTE CHOLECYSTITIS IN THE AGED. A PLEA FOR EARLY SURGERY.

Parrella, G. S. *Connecticut State M. J.* **19:** 377 (May) 1955.

Acute cholecystitis is predominantly a disease of older age groups. Biliary-tract disease is the most common cause for abdominal surgery in the elderly patient. There is no typical course in acute cholecystitis in the aged. Perforation of the gallbladder is more common in this age group than in younger individuals. It usually occurs three or four days after the onset of symptoms of acute cholecystitis. The signs and symptoms of acute cholecystitis in the aged do not reflect the severity of the pathologic findings, and there are no laboratory findings indicative of perforation of the gallbladder. Gangrene and perforation can occur while the patient is under observation and be easily missed. The use of antibiotics does not defer the perforation of a gangrenous gallbladder. For these reasons, early cholecystectomy is the treatment of choice for acute cholecystitis in the aged. The operation should be per-

formed within twenty-four to forty-eight hours after hospital admission. Cholecystostomy may be useful in a few patients, but it should be considered only as a temporary procedure.

MANAGEMENT OF BRONCHIECTASIS IN THE OLDER PATIENT.

Pittman, H. S. *Am. J. Surg.* **89:** 974 (May) 1955.

Bronchiectasis in elderly individuals is usually secondary to other disease in the chest and should be managed medically. The disease is usually bilateral and diffuse. Less commonly it is due to a localized bronchial obstructive process such as endobronchial tuberculosis, bronchial adenoma, a foreign body, or rarely bronchogenic carcinoma. The diagnostic procedures should be individualized, and include: 1) examination of the sputum (a) for tubercle bacilli when the x-ray examination suggests a history of pulmonary tuberculosis or when localized disease could be due to bronchial tuberculosis, and (b) cytologically by the Papanicolaou technic when there is repeated blood streaking, 2) x-ray examination of the chest, taking postero-anterior and lateral films, with the addition of a postero-anterior grid film and a bronchogram if surgery is to be performed, and 3) bronchoscopy, when there is a question of bronchial obstruction and when there is bleeding. Treatment is aimed at the control of symptoms. A dry unproductive cough should be suppressed. Expectorants and postural drainage, when possible, are used for raising secretions. Elderly patients with bronchiectasis are never free from infection in the respiratory tract and are subject to colds. The number and severity of acute infections can be reduced by prophylactic therapy with a sulfonamide (0.5 Gm. of sulfamerazine or sulfisoxazole twice daily) during the season of colds. Therapeutic doses of sulfonamide are not used in any infection because of the possibility of suppressing bone marrow activity, with resultant leukopenia. Bronchodilator drugs (aminophylline orally, and Vaponefrin, Isuprel, and Neosynephrine by nebulizer) are the most useful. Oxygen must be used with caution, that is, sparingly and intermittently for short periods, in the patient with chronic pulmonary disease who is dyspneic and may be cyanotic at rest. Hemorrhage may be an indication for surgery. When it is severe, surgery may be justified even in a poor-risk patient. An illustrative case is presented wherein pneumonectomy was performed for massive hemorrhage after a patient had been managed medically for four years. When non-pulmonary surgical procedures must be carried out in patients with bronchiectasis, the lungs should be made as free of secretion as possible by the measures mentioned, antibiotics given, and preoperative aspiration bronchoscopy performed, if possible, to clear wet lungs in a patient who does not raise secretions efficiently. For a lengthy surgical procedure under general anesthesia, intratracheal ether with bronchoscopic aspiration at the conclusion of the procedure is preferred. The second case presented is that of elective eye surgery in an elderly poor-risk patient, made possible by proper medical management of the bronchiectasis.

AN EXTERNAL CARDIAC PACEMAKER IN THE TREATMENT OF STOKES-ADAMS SYNDROME: REPORT OF THREE CASES.

Rosenfeld, I., and Segall, H. N. *Am. Heart J.* **50:** 749 (Nov.) 1955.

Three men, aged 82, 62 and 54 years, respectively, with Stokes-Adams attacks failed to respond to conventional therapy. With the use of the Zoll cardiac pacemaker, each attack of ventricular arrest could be terminated almost immediately. The first patient died after sixty-three hours, having reached a point at which electrical stimulation failed to cause the myocardium to respond. The second patient was without independent ventricular contractions for a period of ten hours and was maintained for that time by the pacemaker. At the end of that period, he resumed his previous sinus rhythm of 60 beats per minute with right bundle-branch block and first degree heart block. He was discharged improved, returned to work, and after seven months is free of Stokes-Adams attacks. The third patient survived one admission but returned a month later and died after a total of seventy hours' use of the pacemaker. The muscular contractions caused by the stimuli were painful, so

that analgesics had to be used. Skin burns occurred at the site of electrode application but could be minimized by the application of antibiotic ointment. It was found necessary to use increasingly higher amplitudes of current in order to effect a response. The amplitude required to terminate an attack was greater than that required to maintain ventricular contractions thereafter. The independent heart rate during periods of bradycardia could not be influenced by the pacemaker. The sensorium of the patients remained clear if the proper number of effective stimuli were delivered in patients without cerebral damage. The cardiac pacemaker was concluded to be an effective and convenient means of terminating Stokes-Adams attacks. It does not affect the long-term prognosis of the disease. However, if the apparatus is available during an attack, support at this time may result in an indefinite prolongation of life.

THE NATURAL HISTORY OF MENTAL DISORDER IN OLD AGE.

Roth, M. *J. Ment. Sc.* **101:** 281 (Apr.) 1955; through *Digest Neurol. & Psychiat.* **23:** 367 (Aug.) 1955.

The records of 450 patients with mental disorders of late life were studied and classified into five diagnostic groups: *affective psychosis*—patients whose hospital admission had been occasioned by a sustained depressive or manic symptom complex; *senile psychosis*—patients with a history of gradual and progressive failure in the activities of everyday life and a clinical picture dominated by failure of memory and intellect, and disorganization of personality; *late paraphrenia*—patients with a well organized system of paranoid delusions, with or without auditory hallucinations, existing in the setting of a well preserved personality and affective response; *arteriosclerotic psychosis*—patients in whom dementia was associated with focal signs and symptoms indicative of cerebrovascular disease, or in whom a remittent or markedly fluctuating course at some stage of the dementing process was combined with emotional incontinence, the preservation of insight, or epileptiform seizures; and *acute confusion*—patients showing rapidly evolving clouding of consciousness produced by some extraneous cause or appearing for no discoverable reason. Affective psychosis accounted for over half the cases. Follow-up studies showed that at six months and two years after admission each of the five disorders was characterized by a distinctive pattern of outcome as described by the proportion of patients dead, in the hospital, and out of the hospital. The results suggested that affective psychosis, late paraphrenia, and acute confusion are distinct from the main causes of progressive dementia in old age, that is, senile and arteriosclerotic psychosis. They also provide some support for the validity of the clinical distinction drawn between senile and arteriosclerotic psychosis. The relevant differences between the groups were largely independent of differences in age distribution. The overlap between the senile-arteriosclerotic group and the affective-paraphrenic group was relatively small. Few individuals with affective psychosis became demented, and an insignificant proportion of cases of senile and arteriosclerotic psychosis commenced with affective symptoms alone. The incidence of affective symptoms in senile psychosis was low and probably due to chance association. However, more than a quarter of the patients with arteriosclerotic psychosis had affective symptoms. The precise significance of this finding cannot be decided without further investigation. Additional problems for further study are discussed. Investigations into the differences *between* and *within* the groups might lead to the identification of factors of practical or etiologic significance.

MALIGNANT TUMORS OF RENAL PARENCHYMA IN ADULTS.

Royce, R. K., and Tormey, A. R., Jr. *J. Urol.* **74:** 23 (July) 1955.

The recurrence of occasions when an inoperable kidney tumor is encountered during surgery, and the lack of recovery from the morbidity of an operation in patients who have tolerated a tumor for several years, prompted a review and analysis of 102 consecutive cases of malignant parenchymal tumors of the kidney in adults. Among the 75 nephrectomies, 28 were performed in incurable cases. Eight of the patients died following the

operation. Twelve were known preoperatively to have had metastases, and the results in all these cases were bad. X-ray therapy was of no benefit in the 27 nephrectomized patients so treated. The five-year survival rate was 22 per cent, and the rate of apparent cures 18 per cent. Local recurrences appeared to be due to preoperative spread of the tumor rather than to implantation of tumor in the surgical wound. The prognosis was better in the cases of well-differentiated and of smaller tumors. The prognosis did not appear to be related to the duration of symptoms preoperatively, but it was particularly grave if weakness and symptoms indicating distant metastases were present. The patient's age did not significantly influence the prognosis. The presence of dilated perirenal veins was usually associated with an inoperable tumor. These results indicate that more thorough preoperative studies should be made. The removal of kidney tumors that have metastasized is of little benefit and seems to have shortened the life of some patients. The thoraco-abdominal approach is superior to the regular flank and transperitoneal approaches because, by using it, the area of the renal pedicle and vena cava can be inspected before freeing the kidney. If the tumor is found to be inoperable, the procedure can be terminated without having to perform a bloody, useless nephrectomy.

DISTINCTIVE DIAGNOSTIC FEATURES OF MATERIAL ASPIRATED FROM MARROW IN METABOLIC BONE DISEASES.

Rubenstein, M. A. *California Med.* **82:** 440 (June) 1955.

In a series of cases of Paget's disease of the bone, two types of cells not previously described were observed in material aspirated from bone marrow in areas of osteitis deformans. One type was mononuclear, the other was giant, multinucleated and syncytial. They were identified as osteoblasts and osteoclasts, respectively. The identification was based mainly on correlation with the histologic picture of osteitis deformans and of normal-growing bones as seen in section studies. Both osteoblasts and osteoclasts were recovered in aspirated bone marrow material in other instances of metabolic bone diseases associated with increased bone repair and bone resorption—in hyperparathyroidism, osteoblastic malignant lesions, rickets, hemolytic anemia in children, and in normal infants in the growth zone of bone in the tibia. They were not seen in senile and postmenopausal osteoporosis. Recognition of osteoblasts and osteoclasts in smear preparations from aspirated bone marrow material may serve as a diagnostic aid in metabolic bone diseases. The differentiation of osteoblasts from neoplastic cells is important in cases in which metastatic cancer of the bone is suspected and x-ray findings are inconclusive. (Author's summary.)

THE EFFECTS OF AGE ON FINGER TEMPERATURE RESPONSES TO LOCAL COOLING.

Spurr, G. B.; Hutt, B. K., and Horvath, S. M. *Am. Heart J.* **50:** 551 (Oct.) 1955.

Finger temperature measurements were made before, during, and after a period of immersion of the hand in a 10°C. water bath, on healthy individuals varying in age from 6 to 83 years. The hunting reaction tended to occur less frequently with advancing age of the subjects. Similarly the rates of cooling and rewarming of the finger appeared to be influenced by the age of the individual. It is suggested that these differences in response to a local cold stimulus were related to changes in vascular reactivity. (Authors' summary.)

MALIGNANT LYMPHOMATOSIS OF THE KIDNEYS.

Wentzell, R. A., and Berkheiser, S. W. *J. Urol.* **74:** 177 (Aug.) 1955.

Primary renal lymphoma has never been proved. All cases have been secondary to foci elsewhere, usually in the retroperitoneal or mediastinal lymph nodes. No reported case of renal lymphomatosis has been definitely diagnosed preoperatively. Because of these facts, the records of all cases of malignant lymphoma during six years at the Robert Packer Hospital were reviewed. Among 1,047 necropsies, there were 32 cases (3 per cent) of histologi-

cally proved malignant lymphoma. The kidneys were involved in 17 of the 32 cases (53 per cent). The percentages of cases with renal involvement were as follows: lymphosarcoma, 77.7; reticulum-cell sarcoma, 16.6; Hodgkin's granuloma, 20; Hodgkin's sarcoma, 100; multiple myeloma, 100; all leukemias, 60. There were 24 males and 8 females (6 of whom had lymphosarcoma and 2, reticulum-cell sarcoma). All except 6 patients were beyond 50 years of age at the time of death. The signs and symptoms of the various types of malignant lymphoma are reviewed. Genito-urinary symptoms may consist of albuminuria, pyuria, or hematuria—alone, or with dull or colicky pain in a flank or flanks due to progressive hydronephrosis. It is rare for such symptoms and signs to appear alone or early in the course of malignant lymphomatosis. Any patient with slowly progressive renal failure not easily explainable should be suspected of having urinary-tract involvement by malignant lymphoma. The renal failure may be due to lymphoma cell infiltration into intertubular and periglomerular tissues, with resultant pressure degeneration and atrophy. In no case in the series was surgical excision applicable. In the majority of cases the disease is so widespread by the time the patient is seen that therapy can be only palliative. The therapeutic agents suitable for use in various lymphomas include radiation, nitrogen mustard, triethylene melamine (TEM), aminopterin, α-methopterin, 6-mercaptopurine, corticotropin, cortisone, radioactive phosphorus, urethane, and Myleran. The appropriate therapy can make the patient more comfortable and sometimes prolong life.

THE PATHOLOGY OF SENILITY.

Wilson, D. C. *Am. J. Psychiat.* **111:** 902 (June) 1955; through *Digest Neurol. & Psychiat.* **23:** 302 (July) 1955.

Senility, as the term is now used, is a pathologic state distinctly separate from normal aging. Recent data on the pathology of senility are discussed. It has been thought that senile personality changes are related to the function of the cells of the cerebral cortex. A reduction in blood flow and metabolism has been found in senile psychoses (Freyhan, Woodward, and Kety). Fisher believes that thrombosis superimposed upon arteriosclerosis is the common lesion producing senile psychoses. Lipid, nitrogen, and carbohydrate metabolism have been studied in the aged. Albanese and his co-workers found that the utilization of glucose decreases with age, whereas the utilization of fructose is only slightly affected. That constitutional factors also affect old age has been demonstrated by Kallmann and Sander. They found in pairs of aged twins that basic physical and psychologic qualities which were similar tended to persist. They postulated a certain capacity for survival in these twins. Psychologic studies in aged people have showed that they gradually lose flexibility and learning power. Dorken and Kral concluded, after studying senile dementia and arteriosclerosis, that the process of senile deterioration does not depend upon age and that it is selective, in that the individual does not deteriorate in all traits. Psychiatrists have found that depressive, toxic and schizophrenic reactions can be treated successfully in aged persons, but that the act of hospitalization can itself be risky. Patients with simple dementia have a poorer survival rate than those with senile reaction complicated by schizoaffective states. Possibly the presence of neurosis and psychosis acts as a defense against dementing forces which surround the patient, or the ability to act as a schizophrenic or depressed patient indicates that there must be potentials for further living. In the field of sociology, advances have also been made in understanding senility. Loneliness and a feeling of being unwanted and without use in the world are factors in producing senile psychosis. Retirement from active life without having something to retire into is recognized as a mistake. The studies of Busse and co-workers have shown that aged people have the same needs, desires, and reactions as younger people, although with certain modifications. It is concluded that senile change in man is a disease state arising from inherited, biologic, psychologic, and sociologic causes. The pathology of senility exists in all these areas. By combining the efforts of investigators in each, perhaps it can be learned how to prevent the disorder.

NEWS AND NOTICES

FOURTH CONGRESS OF THE INTERNATIONAL ASSOCIATION OF GERONTOLOGY

The Fourth Congress of the International Association of Gerontology will be held in Marano (Bolzano), Italy, *July 14–19, 1957* and will be immediately followed by the International Symposium on Medical-Social Aspects of Senile Nervous Diseases, in Venice, Italy, *July 20–21, 1957*. The Congress and the Symposium constitute a single integrated program.

Membership in the Congress and the Symposium is open to all members of the national societies affiliated with the International Association of Gerontology, as well as to physicians and students who are interested in gerontological problems and research.

The official languages will be English, German, French and Italian.

Address all communications to: *Segreteria, Quarto Congresso Internazionale di Gerontologica, Viale Morgagni 85, Firenze, Italy.*